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MARCH 1959

DISEASES of the CHEST

OFFICIAL PUBLICATION

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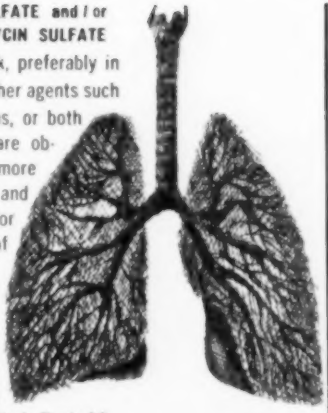

*Committee on Chemotherapy and Antibiotics, American College of Chest Physicians. Present status of chemotherapy in tuberculosis, J. Indiana M. A. 51:799 (June) 1958.

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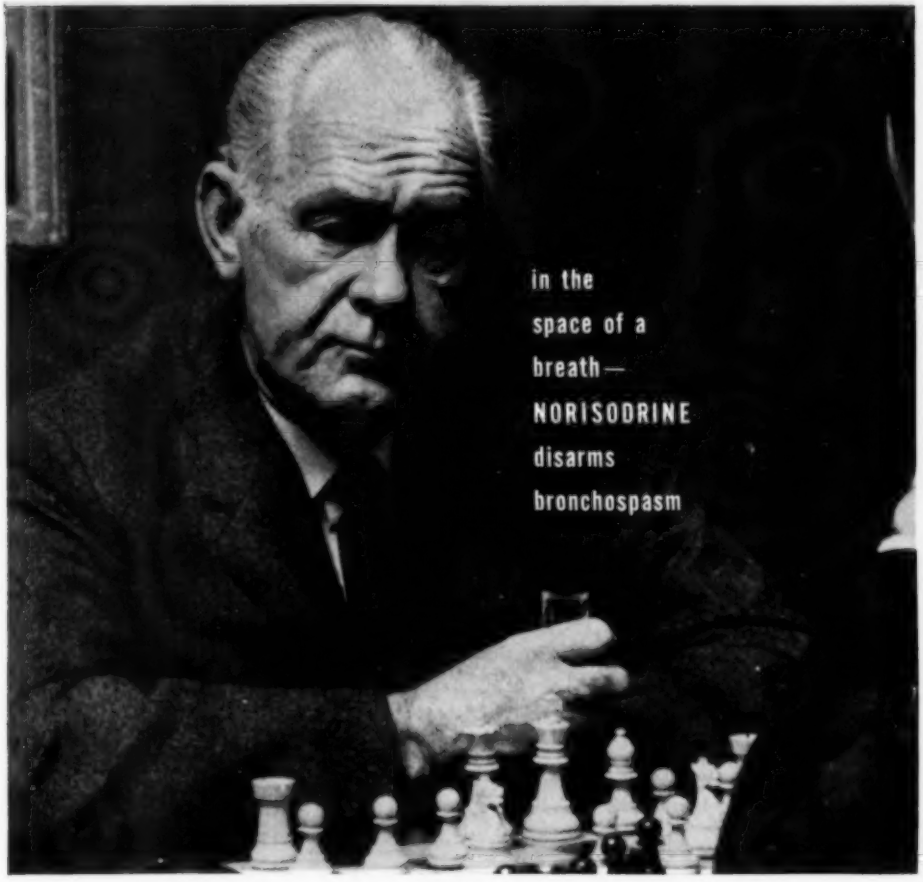

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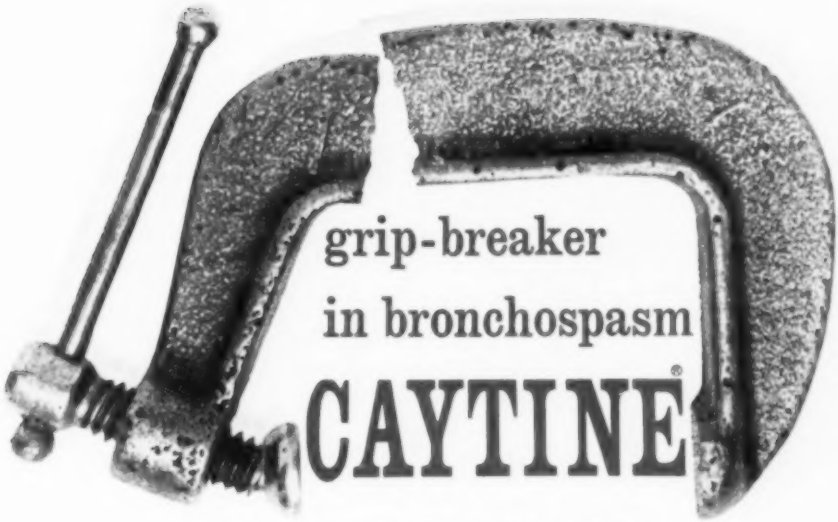

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(1) Leslie, A., and Simmons, D. H.: Am. J. M. Sc. *234*:321, 1957. (2) Settel, E.: Am. Pract. & Digest Treat. *8*:1249, 1957.

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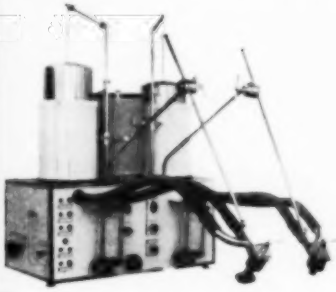

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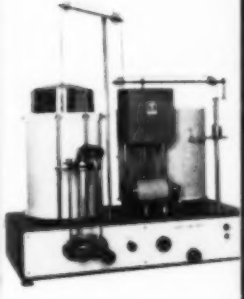

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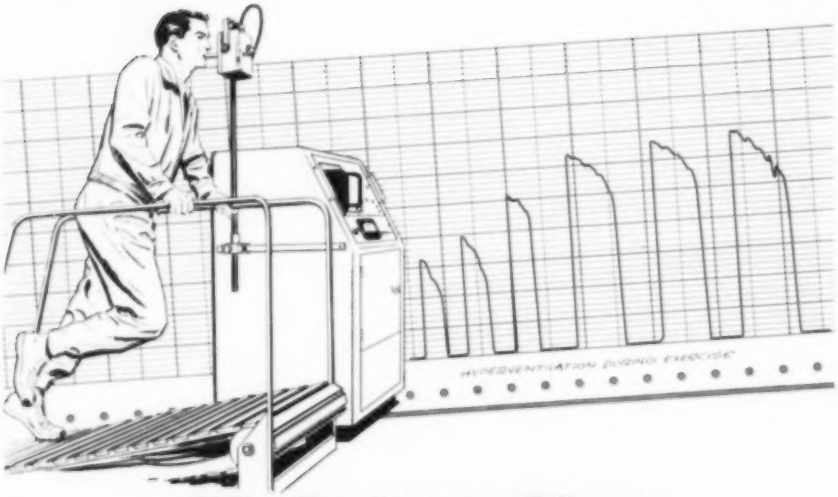

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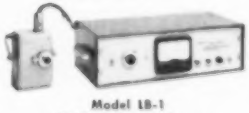

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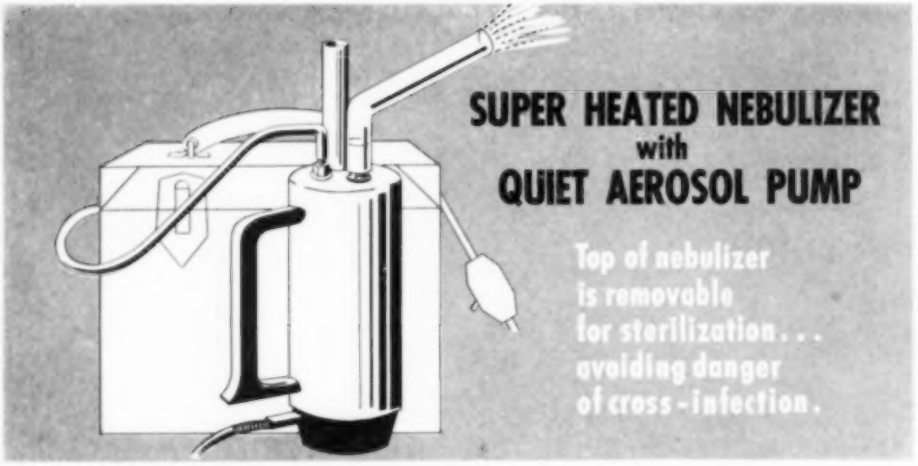

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LEVINE, E. R.: To be published.

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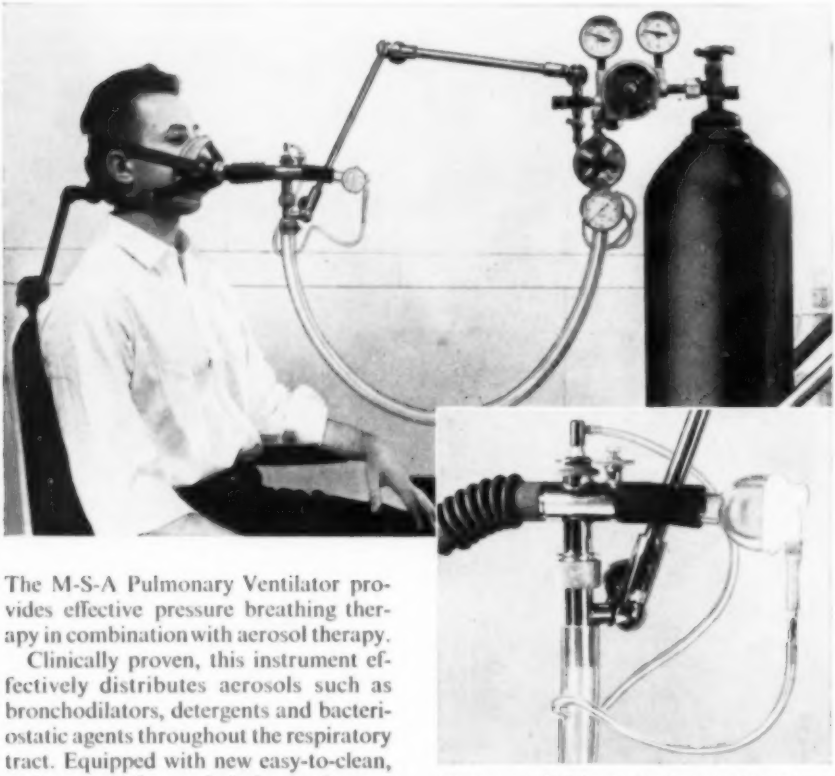

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2. TESSALON acts centrally, to control cough at the level of the "cough center" in the medulla.
3. TESSALON is reported to thin sputum.[1]
4. TESSALON increases vital capacity and ventilation.
5. TESSALON improves exercise tolerance.
6. TESSALON relieves dyspnea.

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Shane and co-workers,[2] using the method of Bickerman and Barach,[3] induced measurable cough in 20 volunteers, using a 15 per cent citric acid aerosol as the cough-producing agent. The antitussive efficacy of TESSALON (100 mg.) was estimated to be 2½ times that of codeine (½ grain) in this test.

Cough suppressing activity of TESSALON[2]

	Average Number of Coughs*
No therapy	8.3
Codeine	4.4
TESSALON	1.7

*Based on 5-minute interval immediately following inhalation of citric acid to induce cough. Each patient was tested on three separate occasions.

Controls cough in the chest

It has been shown that the increased sensitivity of the sensory receptors in the lung during inspiration is an important part of the cough mechanism. TESSALON has a selective inhibiting effect on these dilation or "stretch" receptors[4] that helps to control cough where cough begins—at points of irritation in the chest.

Controls cough at the cough center in the medulla

Spinal reflex arcs were studied for the inhibitory effect of TESSALON on the transfer of afferent cough impulses to the efferent branch of the cough reflex.[5] The administration of TESSALON inhibited reflex transmission, when the afferent nerve was stimulated electrically. With this "damping" effect on the cough center in the medulla, TESSALON controls cough centrally, as well as peripherally.

Thins sputum

TESSALON controls cough frequency without interfering with productivity or expectoration. In fact, sputum is usually thinner, easier to raise.[1]

Effect of TESSALON on sputum[1]

Amount		Consistency	
Less	32 patients	Heavier	3 patients
More	2* patients	Lighter	27 patients
Same	16 patients	Same	20 patients

*These patients noted more but lighter sputum.

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Respiration usually increases both in depth and volume during TESSALON treatment.[6] In one study,[7] patients with chronic respiratory disease, with and without bronchospasm, showed a mean increase of 19.7 per cent in vital capacity after a 2-week course of TESSALON.

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By inhibiting stretch receptor activity, and by increasing air intake, TESSALON enables patients to tolerate exercise or work better, eliminates many paroxysms of coughing.

Relieves dyspnea

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The cough suppressant effect of TESSALON starts rapidly—usually within 15 to 20 minutes. The duration of effect is prolonged—usually from 3 to 8 hours.

Indications

TESSALON is indicated in acute and chronic cough.

ACUTE: Common cold, Bronchitis, Pneumonia, Upper respiratory infection, Pleurisy, Spontaneous pneumothorax, Bronchial irritation provoked by gases and foreign bodies. CHRONIC: Pulmonary emphysema, Bronchitis (emphysematous, asthmatic), Bronchial asthma, Tuberculosis, other chronic pulmonary diseases, Pulmonary or mediastinal tumors

PROCEDURES: Bronchoscopy and bronchography, Thoracentesis, Thoracic surgery

Dosage

ADULTS: Average dosage is one Perle (100 mg.) t.i.d. If necessary, or where cough is refractory, up to 6 Perles (600 mg.) daily may be given.

CHILDREN UNDER 10: One Pediatric Perle (50 mg.) t.i.d. is the usual dosage.

The Perles should be swallowed without chewing, and, if necessary, with a liquid. Release of TESSALON from the Perle in the mouth produces a temporary local anesthesia of the oral mucosa.

Side Effects

TESSALON is well tolerated. Only occasionally have side effects been reported. Skin rash, nasal congestion and a vague "chilly" sensation have been mentioned. In rare instances, gastrointestinal upset, constipation or sedation have been observed. No adverse effects on respiration, kidney or liver function tests, blood count or urinalysis were reported.

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Perle form (liquid-filled gelatin spheres) provides speed of liquid medication—convenience and dosage accuracy of capsule medication. In two strengths: 100-mg. Perles (yellow), for adult use; 50-mg. Perles (red), for children under 10.

Samples available on request.

References

1. Simon, S. W.: Ann. Allergy 15:521 (Sept.-Oct.) 1957. 2. Shane, S. J., Krzyski, T. K., and Copp, S. E.: Canad. M.A.J. 77:660 (Sept.- 15) 1957. 3. Bickerman, H. A., and Barach, A. L.: Am. J. M. Sc. 228:156 (Aug.) 1954. 4. Bein, H. J., and Bucher, K.: Helvet physiol. et pharmacol. acta 15:55 (March) 1957. 5. Meier, R., and Bein, H. J.: Personal communication. 6. Michelson, A. L., and Schiller, I. W.: J. Allergy 28:514 (Nov.) 1957. 7. Bickerman, H. A.: To be published. 8. Farber, S. M., and Wilson, R. H. L.: To be published.

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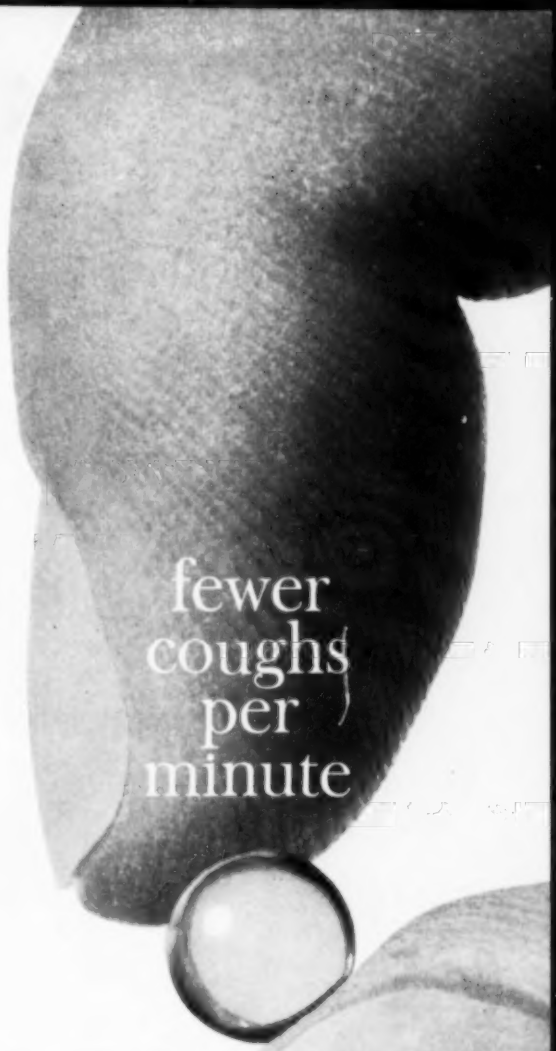

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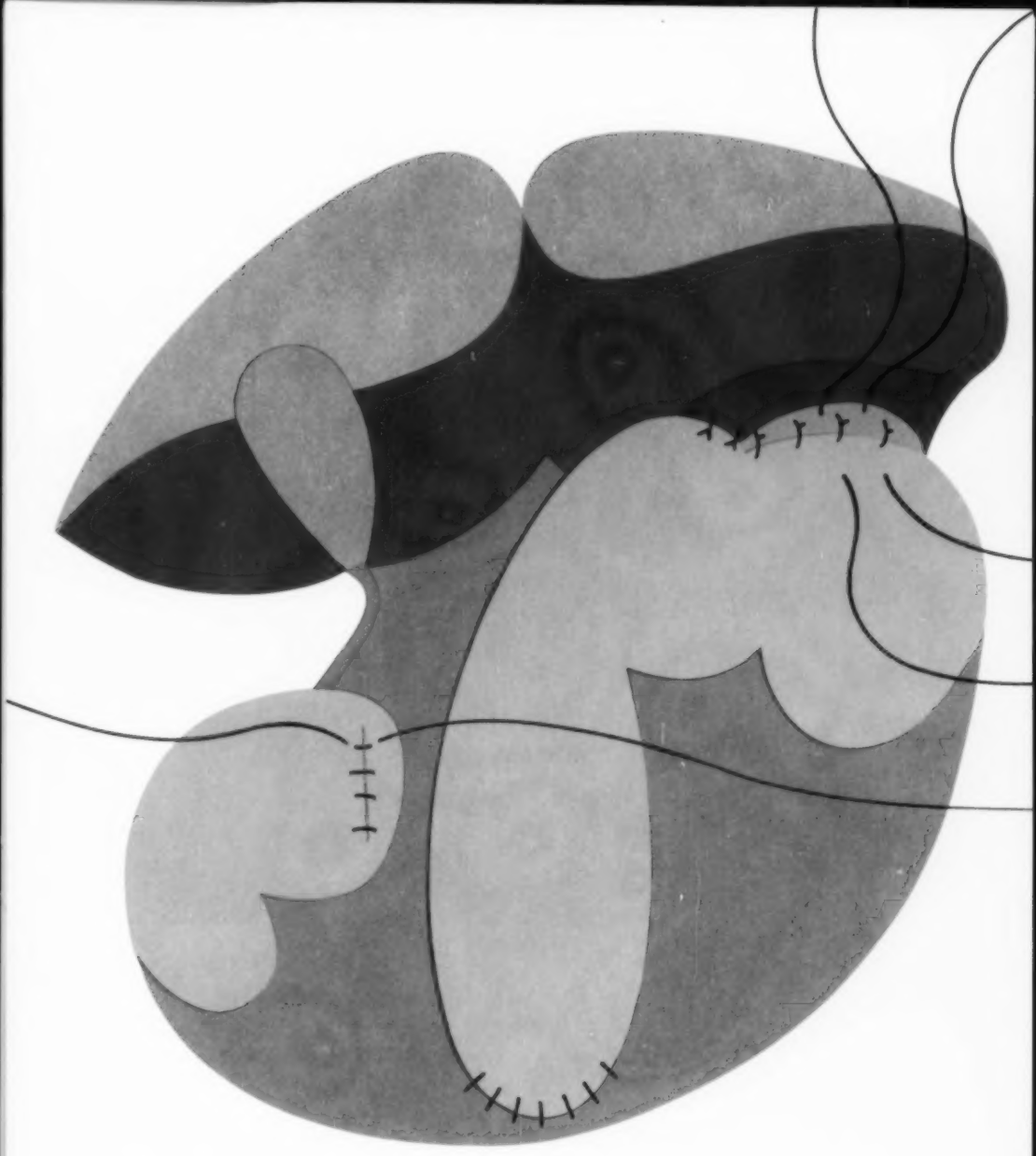

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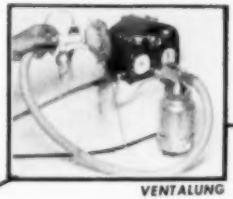

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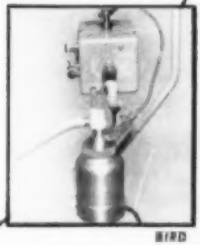

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Considerations in Humidification by Nebulization: Ivan Cushing, MD, and William F. Miller, MD. Diseases of the Chest, Oct. 1958, Vol. XXXIV, No. 4.

An Aerosol Method of Producing Bronchial Secretions in Human Subjects: A Clinical Technique for the Detection of Lung Cancer. Hylan Bickerman, MD, FCCP; Edith Sproul, MD, and Alvan L. Barach, MD, FCCP. Diseases of the Chest, April, 1958, Vol. XXXIII, No. 4.

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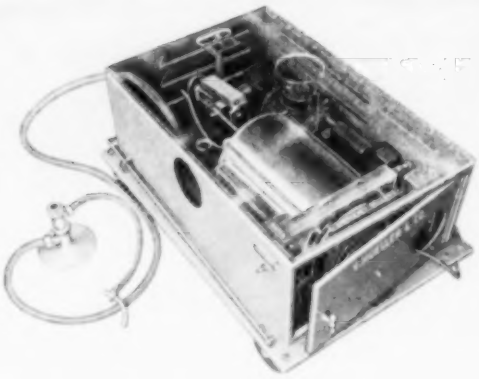

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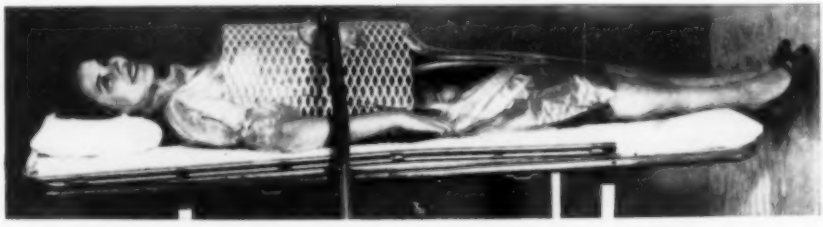

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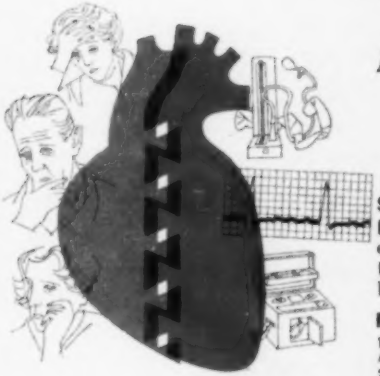

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References:

1. Shapiro, S.: Observations on the use of meprobamate in cardiovascular disorders. Angiology **8**:504, Dec. 1957.
2. Friedlander, H. S.: The role of ataraxics in cardiology. Am. J. Cardiol. **1**:395, March 1958.
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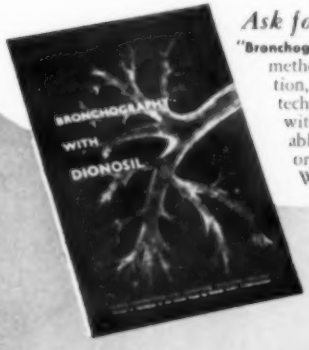

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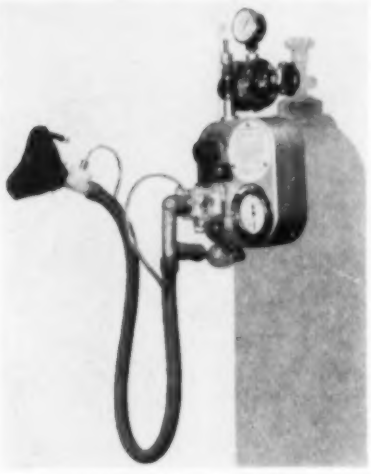

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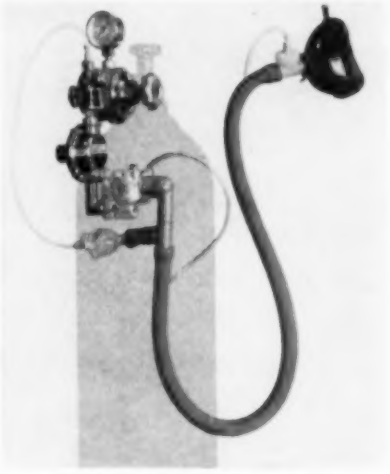

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*Miller, J.B., et al.: Ann. Allergy, 12:611, Sept.-Oct., 1954.

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REFERENCES: • 1. Freyberg, R. H., Bernsen, C. A., Jr., and Hellman, L.: Arth. & Rheum. **1**:215 (June) 1958. • 2. Sherwood, H., and Cooke, R. A.: J. Allergy **28**:97 (March) 1957. • 3. Shelley, W. B.; Harun, J. S., and Pillsbury, D. M.: J.A.M.A. **167**:959 (June 21) 1958. • 4. Dubois, E.L.: California Med. **89**:195 (Sept.) 1958. • 5. Hartung, E. F.: J.A.M.A. **167**:973 (June 21) 1958.

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1. Nussbaum, H. E., Leff, W. A., Mattia, V. D., Jr. and Hillman, E.: An effective combination in the treatment of the hypertensive patient. Am. J. M. Sc. **234**: 150, Aug. 1957.

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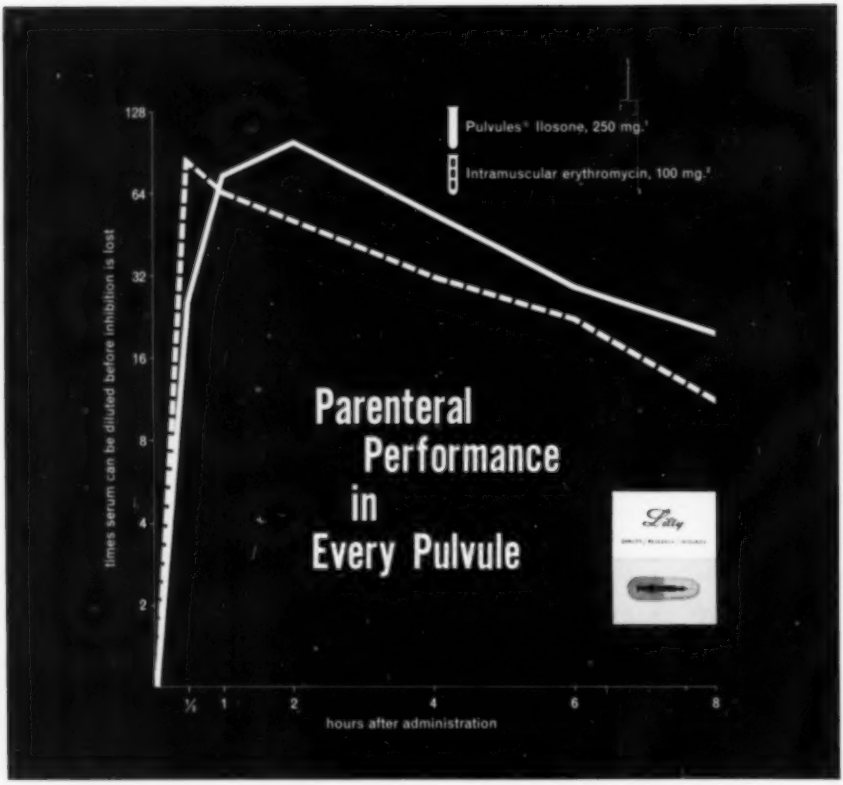

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1. Antibiotic Med. & Clin. Therapy, 5:609, 1958.
2. Data from Antibiotics Annual, p. 269, 1954-1955.

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DISEASES of the CHEST

VOLUME XXXV MARCH, 1959 NUMBER 3

Ambulatory Oxygen Therapy: Oxygen Inhalation at Home and Out-of-Doors*

ALVAN L. BARACH, M.D., F.C.C.P.

New York, New York

The use of oxygen at home was based on the application of respiratory physiology to clinical disorders of breathing, but its recent increased employment is the result of the development of apparatus that is now practical for the patient to handle himself. Oxygen is prescribed for relief of shortness of breath, hypoxia and coronary insufficiency; in addition, for increase of cardiorespiratory reserve by utilizing an oxygen exercise program. The technique of oxygen therapy will be presented, including its use during exercise in clinical states characterized by chronic respiratory insufficiency; reference will be made to oxygen inhalation for patients with coronary disease.

The Oxygen-Exercise Regimen

When we found that inhalation of relatively low concentrations of oxygen relieved shortness of breath during exertion, in patients with pulmonary emphysema, a standardized program of graduated walking exercises was inaugurated in our clinic with the purpose of developing the muscles of breathing, and preventing atrophy of disuse of the body musculature and increasing cardiorespiratory reserve. Since inhalation of 32 to 36 per cent oxygen was adequate for this purpose, a simple technique was readily developed which did not include the use of an uncomfortable mask.[1-3]

During the past 10 years in which walking regimens during the inhalation of oxygen has been employed and found to produce benefit in breathing in more than 100 patients so treated in our clinic, as well as by Cotes et al.[4] in England, and W. B. Miller[5] in the United States, no untoward result has ever been reported. No respiratory depression has been encountered even with inhalation of 40 to 50 per cent oxygen during exercise.

One or more of the apparatus to be described may be employed for the administration of oxygen. A conventional large oxygen cylinder containing approximately 6,000 liters may be obtained from an oxygen therapy service company and installed in the patient's home, with regulator.**

*This presentation contains excerpts from a book in preparation, a *Doctor-Patient Manual for Patients with Bronchial Asthma, Pulmonary Emphysema and Bronchiectasis.* (Williams and Wilkins, Baltimore.)

**There is no charge for the rental of the cylinder, but the patient is billed for the contents of oxygen in it. The oxygen regulator is purchased rather than rented from the oxygen therapy company since it is much less expensive in the long run to own it, as well as the nasal device for inhaling of oxygen, such as the double bent plastic tubes that enter about one-quarter inch inside the nares.

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The use and care of the regulator is of considerable importance. Even though an oxygen technician is employed to change the regulator from one cylinder to another, patients should be familiar with the simple rules involved. The circular wheel at the top of the large cylinder is turned counter-clockwise to blow away any dust that may have accumulated in transport. Under no circumstance should any oil or lubricant be smeared on the thread or any part of the regulator. The regulator is then connected to the tank and made tight by a wrench which is supplied with the valve. Before the oxygen is turned on from the cylinder, by turning the circular wheel at the top of the cylinder, the regulator handle is turned counter-clockwise until it is loose, i.e., in order that no oxygen is delivered when the wheel at the top is turned on. This precaution prevents the full force of oxygen from hitting the valve mechanism or diaphragm inside the regulator.

If a hissing noise is heard at the attachment on the valve, the wrench is employed again to tighten it further. The regulator handle is now turned clockwise until 1, 2, 3, 4, 15, or whatever flow of oxygen, in liters per minute is desired. An oxygen humidifying bottle may be attached to the regulator but it is a needless expense. (Some of the oxygen water bottles leak and oxygen may be lost thereby.) For periods as short as those

FIGURE 1: Light weight oxygen cylinder with double nasal plastic tubes.

involved in an oxygen-exercise program, the dry oxygen inhaled has no decipherable effect on the mucous membrane of the nose or pharynx.

A 50 foot length of rubber tubing is generally used in the oxygen-exercise program. Light rubber is preferable to gum tubing, although a good texture of plastic tubing may also be firmly attached to the regulator and to the device for inhaling. If powder is present in the tubing a thorough cleansing with water should first be used. The facial attachment to the rubber tubing consists of a double plastic cannula that is currently in use. Many years ago a metal curved nasal cannula was used; later we employed a rubber nasal tube shaped by wire in the wall, or molded to enter into the nostril about one quarter of an inch.[4] Recently, plastic tubes have been made, like the Hudson or other make, attached either by an elastic or rubber band or by an eyeglass setting to hold the cannula in place. If the nasal tube is set correctly, so that the oxygen is delivered toward an open aperture in the nose and not so as to strike the mucous membrane above or below, the inhalation of oxygen by this method is more comfortable to most patients than by any other type of oxygen therapy apparatus. The oxygen flow from the large cylinder runs continuously, although demand type oxygen or oxygen inhaled during inspiration may also be provided, even at times with a mask. The nasal

FIGURE 2: Varieties of Oxy-Hale apparatus provide from 3 to 24 liters of pure oxygen, 21 to 168 liters of 32 per cent oxygen at sea level, or 30 to 240 liters of 100 per cent oxygen, saturated with water vapor at 37°C., at 30,000 feet altitude.

tubes and oxygen apparatus used in inhalation therapy is shown in the accompanying illustrations.[5] (See Figs. 1 and 2.)

When oxygen is inhaled for exercise from a large cylinder its cost is so small that it is considered convenient to allow it to run during inspiration and expiration. When the small, portable Oxy-Hale apparatus is employed, the regulating valve is turned on during inspiration only.

In patients who are short of breath, a flow of 8 liters per minute is used at the start of an oxygen-exercise program. In the majority of cases 6 liters per minute is adequate; after the program has been in effect for two or three weeks or more, 4, 5 or 6 liters of oxygen per minute may permit exercise to take place without undue increase in the volume of air breathed. The actual percentage of oxygen in the air inhaled varies considerably, depending upon the volume of the ventilation per minute, i.e., the amount of air inhaled. At an *inspiratory* flow rate of 20 liters per minute, 4 liters per minute would theoretically provide 36.8 per cent oxygen. In dyspneic patients 4 liters per minute flow would almost always provide above 28 per cent oxygen in the inspired air, 6 liters above 32, 8 liters above 38, and 10 liters above 40 per cent oxygen. The physician directing the program will prescribe the liter flow of oxygen desired.

When 8 liters per minute is used, the average patient may begin by walking 50 steps back and forth across the room, carrying the oxygen tubing in his hands. When this walking exercise is concluded, he should breathe oxygen at rest for 5 minutes, then walk half the amount, viz. 25 steps, breathing air and rest at the conclusion of this walking exercise with air. If he finds himself quite short of breath, he should reapply oxygen at a flow of 4 liters per minute, for 2 to 5 minutes, which is adequate to relieve the lack of oxygen (or oxygen debt) that might be produced by walking in the air atmosphere.[7-10] In addition, manual compression of the lower chest, as previously described,[1-3] is frequently helpful to reduce alveolar overdistention. In addition, prior to exercise it is helpful to inhale a bronchodilator aerosol, such as 2.5 per cent racemic epinephrine (Dylephrin) or 0.4 per cent isoproterenol with 2.0 per cent phenylephrine (Nebu-Prel).*

Graduated exercise with oxygen is generally followed by increased exercise capacity breathing air. In our clinic the number of steps is usually doubled every day or every third day until 700 steps are walked twice daily. Some individuals are more comfortable by maintaining this degree of walking with oxygen, with half the number of steps breathing air for a period of several weeks, or until sufficient cardiorespiratory reserve has been developed to prevent undue shortness of breath or palpitation. From 700 steps to 1,000 steps, the increase in daily walking is changed at weekly intervals. If the patient is unable to walk one half the number of steps in air without undue shortness of breath, he is told to stop at that point where breathing difficulties begin, and to inhale oxygen at 4 liters per minute for five minutes after exercise with air.

The oxygen exercise program is never carried out after eating, but preferably one hour to half an hour before eating, thus, in the late morning and in the late afternoon. As a rule, two sessions a day of walking

*Made by Irwin Neisler Co. and the Thomas J. Mahon Co.

are employed although in some instances, the patient may wish to walk three times daily, which is all to the good.

Although higher concentrations of oxygen with relatively smaller liter flows of oxygen are obtained in mask oxygen therapy, there is at the present time no comfortable mask or face tent available for this purpose suitable to the majority of patients. However, in some instances a light plastic device may be found useful. Research is now in progress aimed at the development of a new type of breathing apparatus that will be more comfortable for this purpose.

The Light Weight Oxygen Cylinder

A two and three-quarter pound oxygen cylinder containing approximately 180 liters of oxygen under 1800 pounds pressure has recently become available.* The advantage of a light-weight cylinder of this kind is that the patient may have a total of one-half hour of walking exercise at 6 liters per minute. In a number of instances 4 liters per minute may be sufficient to enable the patient to walk at a moderate rate without shortness of breath. This 4 liter flow to a mask has been used by Cotes and Gilson[4] in England for an exercise program. The cylinder, strapped over the shoulder or over the neck of the patient, hangs at the side with the regulator set at the flow desired. When the cylinder has been emptied, it may be refilled from a large high pressure cylinder up to a pressure of approximately 1800 lbs. per square inch. This may be done by an oxygen company or by an inhalation therapy service technician, or by the patient himself trained to do so. The process is simple: the small cylinder may be refilled seven times before the pressure drops below 1800 p.s.i in the larger cylinder.

The oxygen cylinder is first turned to expel any dust that may be in it and the low pressure light cylinder is then screwed into a fitting attached to the large cylinder and then attached by a wrench. The large circular wheel at the top of the high pressure cylinder is turned on gently and oxygen allowed to flow into the light-weight cylinder until the pressure of 1800 pounds per square inch is registered on the dial; it is then turned off, the light-weight cylinder unscrewed from the attachment provided for refilling and the oxygen valve attached to it. The valve at the top of the light-weight cylinder is automatically closed when it is released from the cylinder attachment.

These light-weight cylinders are also convenient for patients to take along on automobile trips, visits to the doctor or for x-ray when intermittent or continuous oxygen is required. A flow of 4 liters per minute of oxygen is adequate for the large majority of patients with pulmonary emphysema and a cylinder of this kind is easily carried by the patient himself, a relative or nurse. Two of them would, of course, give an hour and a half of continued treatment if necessary. It is also true that two liters per minute of oxygen is adequate to give a certain number of cases of pulmonary emphysema relief from burdensome dyspnea when at rest. These cylinders are also preferable to the heavier type of cylinders employed in hospitals to bring patients from the room floor to x-ray or to the

*This cylinder is supplied by Controlled Pressure, Inc., Erie, Pennsylvania. It is imported from England. A similar cylinder will be made here.

operating room when indicated. However, still smaller equipment may be used if oxygen is employed during inspiration only, as is described in the next section.

High Portable Oxygen Therapy Equipment
The Oxy-Hale

The Oxy-Hale is a device with one cylinder somewhat larger than a fountain pen and may be conveniently carried in a man's pocket or a ladies' handbag; a 3-liter oxygen cylinder under 5,000 pounds pressure is used. This device is also available with 3, 5 and 8 cylinders providing 9 to 24 liters of pure oxygen. Attached to the cylinder case is a venturi or a mixing device whereby the three liters of oxygen may draw in 3 to 18 liters of air (or more), thus increasing markedly the total volume of oxygen-enriched air available for inspiration.

The CP oxygen cylinder* contains 3 liters under 5,000 pounds pressure per square inch (p.s.i.). Other gases, such as helium 80 per cent and oxygen 20 per cent, carbon dioxide with and without oxygen, may also be employed for different purposes. The escape of oxygen is into a venturi which provides various admixtures of air in the oxygen stream, depending on the size of the openings. The sleeve arrangement shown in the picture of the apparatus may be moved to various positions.

The aim of treatment is to supply a pre-mixed oxygen-enriched atmosphere of sufficient volume to be effective and comfortable. The subjective feeling of the flow of this air into the mouth (or nose) provides a sensation of treatment in action, as it were, that is not accomplished when 1, 2 or 3 liters per minute are inhaled in a mask. In table I the volumes of oxygen-enriched atmospheres are shown for the various

*The device called "Oxy-Hale" is manufactured by Controlled Pressures, Inc., Erie, Pa.

TABLE I
VOLUME OF AIR-OXYGEN MIXTURES DELIVERED AT MOUTHPIECE OF VENTURI AT VARIOUS PRESCRIBED OXYGEN CONCENTRATIONS

Oxygen Concentration Prescribed	Air Intake per 1 liter of oxygen Flow	Volume of Air-Oxygen Mixture Provided by		Indications
Per Cent	Liters	3 Liters 1 Cylinder	9 Liters 3 Cylinders	
26	16	51	153	Altitudes to 10,000 feet
28	11	36	108	Dyspnea at rest
32	6.1	21	63	Walking exercise (emphysema, etc.)
40	3.1	12	36	Anginal pain, dyspnea due to exertion (emphysema)
45	2.3	10	30	More severe cardiac or respiratory insufficiency
50	1.7	8	24	

concentrations provided, in a 3 liter and 9 liter apparatus. Thus, at a concentration of 32 per cent, the 3 liter cylinder supplies 21 liters of mixed gas at the mouthpiece end of the venturi. If the patient's inspiratory flow rate is 20 liters per minute, and the valve is turned on in inspiration, the duration of use of one cylinder would be 2 minutes, assuming that the flow of oxygen plus air from the venturi is at 20 liters per minute. If 40 per cent oxygen is inhaled and the patient's inspiratory flow rate increased to 24 liters per minute, a single cylinder would last one minute and the three cylinder device 3 minutes, at a flow rate of oxygen plus air of 24 liters per minute from the venturi. The 8 cylinder apparatus, or the use of 8 cylinders, would supply 168 liters of 32 per cent oxygen. With a supply of 10 or 15 cartridges, treatment could be maintained for longer periods, or perhaps until continuous oxygen therapy could be obtained, if needed.

The unit is produced in Anodized Aluminum in a glossy green finish which is the code for oxygen. It can be sterilized in alcohol or in regular autoclaves.

A concentration of 32 per cent oxygen is adequate to relieve the shortness of breath of most patients with pulmonary emphysema. However, if the patient is being treated for more severe lack of oxygen or cardiac pain, approximately 40 per cent oxygen is employed by setting the venturi sleeve on the No. 4 dial; since the one-cylinder apparatus would last one minute when inhaled during inspiration at an inspiratory flow rate of 24 liters per minute, another cylinder or two may be used, the replacement time taking 8 seconds. When a 3 or 5 cylinder apparatus is used, one cylinder is used until empty, then the second turned on.

Although the relief of shortness of breath on inhaling oxygen is greater in pulmonary emphysema than in other chronic pulmonary diseases, there is some relief in conditions such as the granulomatous and fibrotic conditions of the lung; an oxygen-exercise program may be employed in these conditions as well. The Oxy-Hale apparatus is particularly suitable for patients who are traveling short distances and who wish to be relieved promptly of exertionally induced shortness of breath. The highly portable nature of this equipment makes possible visits to the doctor, or to friends, or to the theatre, or a variety of excursions where shortness of breath is precipitated by moving about, but is relieved promptly by inhalation of oxygen. Since five or six cylinder may be taken along, and the cylinder changed quickly, the practical nature of this device for the purposes for which it is intended is apparent. The use of oxygen inhalation in the treatment of coronary insufficiency and at high altitudes will be discussed below.

Although periods of rest are indicated for the patient with chronic pulmonary disease, especially after meals, exercise is unquestionably of very real value in preventing atrophy of the voluntary muscles as well as those involved in breathing, the involuntary muscles of respiration. It is also of considerable importance to encourage these patients to take excursions that will contribute to their enjoyment and interest in life. An apparatus such as the Oxy-Hale is of particular value in allaying apprehension in making expeditions away from home. Its use is quite simple since the patient only needs to learn to close his lips over the

mouthpiece and turn the regulator on while inhaling as slowly and deeply as possible, and turn it off during expiration.

Although the physiological basis for the use of oxygen has been reviewed in recent years[1-4, 6] the following discussion is relevant to the ambulatory use of oxygen.

It was mentioned above that earlier studies showed that the patients with pulmonary emphysema were frequently in oxygen debt, that is to say, so lacking in oxygen that when given oxygen to breathe after exertion they consumed considerably more oxygen than when breathing air for two to five minutes.[7-10] However, an understanding of the importance of lack of oxygen in this condition is not generally appreciated. Inhalation of oxygen is often of critical value in the treatment of heart failure, either secondary to pulmonary disease, arteriosclerotic or coronary heart disease, as well as in the treatment of coronary thrombosis and anginal pain. It is also known that lack of oxygen is the cause of anginal pain and that it plays a significant role in the production of pulmonary hypertension which precedes heart failure in pulmonary emphysema.[18]

Oxygen therapy is indicated at times at rest but it is important to realize that the deficiency of oxygen in the blood and the tissues and inability to increase pulmonary blood flow [6, cf. Motley] incapacitates patients from walking or simple exercise without burdensome dyspnea and/or overdistention of the lungs; inhalation of oxygen in these cases while walking at a moderate pace not only provides oxygen for prevention of dyspnea but also offers an opportunity for the development (by exercise itself) of a significant enhancement of cardiorespiratory reserve, with the ultimate gain of permitting more exercise at rest without the same degree of shortness of breath that was previously present before the exercise program was used.* In recent studies with Bickerman and Beck, the relief of dyspnea has been correlated with a decrease in pulmonary ventilation. Thus, as seen in Figure 3, in a patient who was tested in this respect before and after a 2-step test, the minute volume of respiration at rest was 7.9 liters, after exercise breathing air 16.6 liters and after breathing oxygen 11.1 liters. In each instance the ventilation was recorded while inhaling air.

In the previous studies referred to, the O_2 consumption breathing oxygen had been found to be substantially increased over that recorded when air was breathed. It is noteworthy that the pulse rate is consistently lower when oxygen is breathed during exercise, as has long been known even in normal subjects.

Inhalation of oxygen at high altitudes is now required in jet airplane flight for possible emergency use. The administration of far smaller oxygen flows than are used in the treatment of hypoxia in clinical illness

*It is desirable that the patient be at the most optimal physiological state before the exercise program is carried out. Thus, the stomach should be empty and, in addition, a bronchodilator aerosol should be used immediately before the walking oxygen exercise program is undertaken. This can be done either with a hand bulb nebulizer or by means of one of the devices employed for the inhalation of bronchodilator aerosols.

It is also of interest to mention the favorable effects of exercise on men between 45 and 70 as reported to the Royal College of Physicians this year (1958) by Dr. Jeremy Morris: "Like many entities with an apparent bearing on coronary heart disease, the exercise factor seems to protect against the disease particularly in the earlier part of middle age—the prime of life."

could be provided for each passenger in the Oxy-Hale portable apparatus.

The expansion of gas as a result of reduced barometric pressure is a critical factor in determining the oxygen concentration and oxygen flow needed. The average individual will tolerate a degree of lack of oxygen equivalent to a 10,000 foot altitude for short periods without any ill effect. An illustration of the use of small flows of oxygen may be seen in accompanying Table II, in which it is shown that a flow of 1.57 liters per minute of dry oxygen will provide 93 per cent in the inspired air and a total flow of 10 liters saturated at 37°. This same flow of oxygen, viz. 1.57 liters per minute (at sea level, 760 mm. Hg, dry, 37°) will provide 10 liters of 100 per cent oxygen saturated with water vapor at 37° at an altitude of 36,000 feet, in this instance providing an oxygen tension equivalent to a 5,000 foot ceiling. Even less oxygen could be used to provide a 100 per cent oxygen concentration at 39,500 feet; 1.28 liters per minute will expand to 10 liters of gas saturated with water vapor at 37° F., providing an oxygen tension equivalent to a 10,000 foot altitude.*

The basal pulmonary ventilation of an adult is between 4 and 7 liters per minute. If we assume a moderately increased ventilation of 10 liters per minute the liter flows mentioned above would be adequate to provide equivalent altitudes of 5,000, 8,000 and 10,000 feet as described, either in a demand apparatus or an apparatus in which a collecting bag was used to store the oxygen provided. Under these circumstances an assumption is made that the inspiratory flow rate would be 20 liters per minute. If the individual is breathing at a higher ventilatory flow rate the oxygen required would be proportionately increased.

In planning for emergency oxygen use at altitudes in the neighborhood of 30,000 to 35,000 feet, it will be seen in Table II that the provision of 1.3 liters (760 mm. Hg., 37° dry) per minute of oxygen would give the individual a ceiling equivalent to 10,000 feet. The liter flows of oxygen required to provide a 10,000 ft. atmosphere would vary from 0.3 to 1.3 liters per minute between 15,000 to 35,000 feet. If the supply of oxygen was above this basic requirement, it would make allowance for an increase in ventilation or else provide an oxygen tension equivalent to a lower altitude if the individual was breathing at 20 liters flow rate during the inspiratory cycle. Therefore, 1.4 to 1.6 liters per minute of oxygen

*To convert dry gas volume at any altitude to saturated gas, the following formula may be used:

$$\text{Volume dry} \times \frac{\text{Bar (altitude)}}{\text{Bar (altitude)} - 47} = \text{vol. sat. } 37°$$

Thus, 1 liter of dry gas at sea level = 4.57 liters at 36,500 feet

$$\text{And } 4.57 \text{ dry} \times \frac{166.4}{119.4} = 6.4 \text{ liters sat. } 37°$$

Therefore, each liter dry gas at 37° at sea level will become 6.4 liters of sat. gas 37° at 36,500 feet.

If the pulmonary ventilation is 10 liters per minute (inspiratory flow rate 20.1.p.m.), we can calculate the O_2 flow as wollows:

$$\frac{10.0}{6.4} = \frac{X}{1} \quad \text{or } X = 1.57 \text{ liters.}$$

This oxygen flow will provide a ceiling equivalent to 5,000 ft. A similar calculation indicates that a pulmonary ventilation of 12.4 liters will provide an altitude equivalent of 10,000 feet, with a similar flow (1.56 liters).

from the oxygen cylinder would be an adequate flow if used with a collecting bag and a mask.

As an airplane descends to altitudes lower than 35,000 feet, the advantage of gas expansion diminishes, but the requirement for high oxygen concentrations likewise decreases. A concentration of 33 per cent oxygen provides an altitude equivalent to 10,000 ft. if the plane is at 20,000 feet. This concentration of oxygen may be obtained with a venturi in which 1 liter of oxygen is mixed with 5.5 liters of air. Although an 0.61 liter oxygen flow would supply an adequate oxygen tension, a total flow of oxygen-air mixture would have to be provided by an inspiratory valve on the mask that would open at a slight negative pressure. A total flow of oxygen plus air of 6.5 liters per minute would provide 33 per cent oxygen. In order to produce an inspiratory flow rate of 10 liters per minute, an inspiratory valve on the mask would be provided; this would open to the atmosphere when the volume of the oxygen-enriched atmosphere was insufficient to meet the ventilatory needs of the individual. At this altitude under consideration, viz. 20,000 feet, 1.4 liters of oxygen mixed with 7.7 parts of air would provide a ceiling equivalent of 10,000 feet, in terms of oxygen tension.

The question of security at altitude in respect to oxygen supply may be discussed in the light of the provision of an oxygen flow in excess of

TABLE II

VOLUME OF O_2 (760 mm. Hg. 37° dry) WHEN MIXED WITH AIR AT VARIOUS ALTITUDES TO YIELD 10 LITERS OF MIX (sat. at 37°)

Altitude Feet	Sea Level Equivalent		5,000 ft. Equivalent		8,000 ft. Equivalent		10,000 ft. Equivalent	
	O_2 per cent	O_2 volume	O_2 per cent	O_2 volume	O_2 per cent	O_2 volume	O_2 per cent	O_2 volume
Sea Level	21	—	—	—	—	—	—	—
5,000	25	.29	21	0	—	—	—	—
10,000	31	.73	26	.40	23	.09	21	0
15,000	39	1.14	32	0.71	28	.45	26	.32
20,000	49	1.43	41	1.00	36	.78	33	.61
25,000	63	1.63	52	1.24	46	0.97	42	.81
30,000	84	1.89	69	1.47	61	1.24	56	1.02
33,000	100	2.00	82	1.51	72	1.31	67	1.16
35,000			93	1.57	83	1.33	76	1.24
36,100			100	1.61	89	1.34	81	1.24
36,500					100	1.57	83	1.24
39,500							100	1.28

NOTE: Ventilation of 10 l/min. ambient pressure and saturated 37° are assumed at each altitude shown; since gas will be fed only during inspiration (approximately ½ the time) each of the figures shown should be multiplied by 2, to obtain velocity or flow rate. With collecting bag, 10 liters per minute will provide flow rate needs, i.e., 20 l/min. for ½ minute. In addition, in a demand system 20 liters per minute flow rate will be provided by a 10 liter per minute total flow, since inspiration is calculated to take one-half minute. Thus, a 1.33* liters per minute O_2 flow up to 35,000 feet and a 1.57* liters per minute oxygen flow up to 36,500 ft. will be adequate to provide an 8,000 ft. altitude equivalent atmosphere, with the subject's minute ventilation being 10 liters per minute.

*Sea level pressure.

that required under the circumstances outlined, namely to compensate for hypoxia at altitudes between 15,000 and 36,000 feet or even as high as 39,500 feet. If the disposable cylinder unit was employed with a collecting bag and an inspiratory inlet valve that would only open when the bag was collapsed, any oxygen inlet flow above 1.4 liter oxygen flow could be instituted when needed at high altitudes and maintained until a lower altitude was reached.

As will be seen in Table II, an oxygen flow of 1.4 liters per minute between 30,000 and 39,500 feet would be adequate to supply a pulmonary ventilation of 10 liters per minute as well as enough oxygen to overcome the decrease in oxygen tension in the atmosphere. Between 10,000 and 30,000 feet, a flow of 1.4 liters per minute oxygen would be sufficient to provide the oxygen concentration required to overcome hypoxia but the system would then make use of dilution of air from the atmosphere obtained by the operation of the inspiratory valve attached to the mask.

A 4-cylinder Oxy-Hale apparatus, supplying 12 liters of 100 per cent oxygen, would provide 8½ minutes oxygen inhalation at a 1.4 liters per minute flow; if the oxygen flow were increased twenty per cent, i.e., to 1.7 liters per minute (to compensate for an increase in ventilation), the 4 cylinder apparatus would last 7 minutes.

An additional calculation provides information as to the safety of the oxygen flows if the ventilation of the individual reached double that of the average basal ventilation; namely, 12.5 liters per minute. If an oxygen flow of 1.2 liters per minute were provided under these circumstances, the oxygen tension in the inspired air would always be above that needed

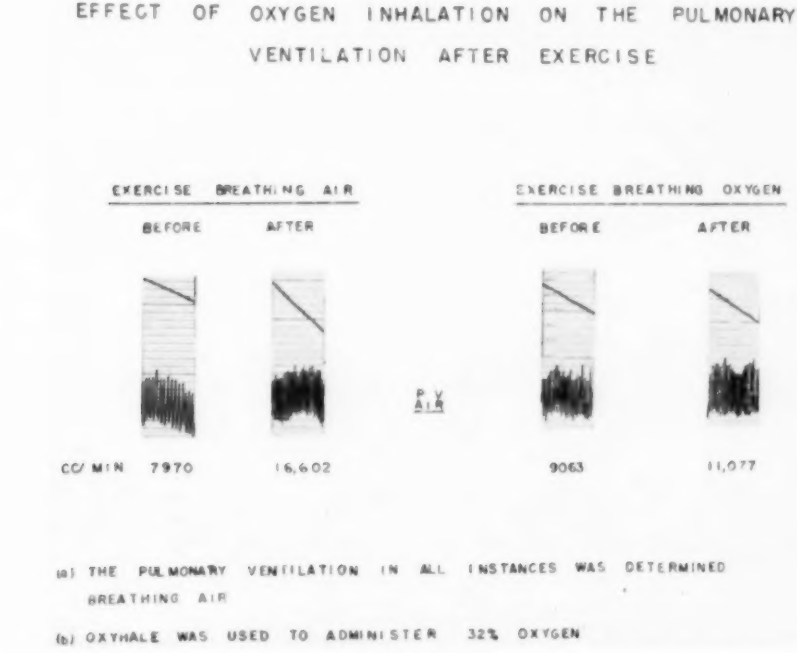

FIGURE 3

for a 14,000 feet ceiling. An oxygen flow between 0.42 and 0.96 liters per minute would give an altitude equivalent of 14,000 feet between 20,000 and 30,000 feet at 12.5 liters per minute ventilation; oxygen flows between 0.34 and 0.77 liters per minute would be needed with a 10.0 liter per minute ventilation. The oxygen flow administered above these requirements would increase the O_2 tension in the atmosphere to levels in effect providing altitude equivalents nearer 10,000 feet, as seen in previous talks.

In the event that the subject should ventilate with an inspiratory flow rate as much as 40 liters per minute, an oxygen flow of 2 liters (dry 760 mm. Hg) would be an additional safety measure. This high flow would be all the more appropriate in the case of sudden decompression of a cabin in which case it would be desirable to take six deep breaths rapidly to wash out the air in the lungs.

Reference may be made to a considerable literature on the use of oxygen in the treatment of coronary insufficiency and thrombosis and anginal pain;[18] these studies are now applicable to the use of more portable oxygen equipment than has been hitherto available. Current investigation is concerned with the employment of the Oxy-Hale device for the relief of anginal pain and related types of coronary insufficiency.

SUMMARY

The use of new types of portable oxygen apparatus which are adapted to ambulatory oxygen is described. The relief of dyspnea on exertion in patients with pulmonary emphysema and related clinical disorders characterized by chronic respiratory and cardiorespiratory insufficiency at home or in the street by the pocket Oxy-Hale device is discussed. The employment of ambulatory oxygen inhalation in patients with anginal pain and coronary insufficiency, as well as in high altitude flight, is presented.

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The Present Situation of Intrapleural Pneumothorax and Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis

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Intrapleural pneumothorax (Pnx) conceived by Forlanini has been considered as one of the most efficacious means in the medical treatment of pulmonary tuberculosis. Numerous statistics, contributions and work performed on this subject by the medical scientists of the whole world, but chiefly European, bear witness to it, testifying the hundreds of thousands of persons kept alive by this therapeutic method, during almost a half century.

Furthermore data support the improvement of pneumothorax results, as the years passed, for example, the recoveries from 15-16.5 per cent reported in 1921 by Niederhauser and Harcus to that of 34-36.2 per cent of Dumarest and Unverricht in 1923, of 49-51.5 per cent of Maendel and Gravesen in 1924, of 48.5 per cent of Naveau in 1925, of 66 per cent of Neumann and Wolf in 1927 and at last of 56.3 per cent of the American authors Allen and Kelly.

Therefore on the basis of a number of clinical investigations we have objectively analyzed 1762 cases of pneumothorax treated at the "C. Forlanini" Institute of Rome, from 1935 to 1953 and followed for at least two years after treatment, was discontinued.

The cases were divided into two groups, one including 1193 treated before antituberculosis drugs from 1935 to 1946, the other 569 from 1947 to 1953 when drugs were available.

The former group was subdivided into those treated between 1935-40 and those between 1941-46.

We divided the data into three groups numerically nearly equal in order to draw a better comparison among them; to better evaluate the evolution in the indications and behaviour of pneumothorax, the latter substantially altered because of the more frequent use of intrapleural pneumolysis and to consider the influence exerted by the war, whose incidence in Italy, with regard to feeding and physical and psychical conditions of the patients ought not to be undervalued.

In the first graph (See Figure 1) one sees the percentages of deaths from any cause occurring during and following pneumothorax treatment from 1935 to 1946.

In the second graph (Figure 2) are the percentage of recoveries and deaths after at least two years following the discontinuance of collapse-

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therapy on subjects belonging to the same period of time. Mortality in the two groups was 15.4 per cent and 9 per cent respectively, and recoveries 66 per cent and 58.9 per cent.

Thus, our data reveals the efficacy of intrapleural pneumothorax in the pre-antituberculosis drug period from 1941 to 1946.

The progressive improvement of results observed by us, and others was due to more careful selection of cases, better technique, and increased use of intrapleural pneumolysis.

As for the indications, efficacy of treatment increased from 48.51 per cent in 1935-40 to 74.4 per cent from 1941 to 1946.

Better selection of patients and improved technique, account for the remarkable decrease of complications during the second pre-antibiotic period (Figure 3).

From 35.2 per cent of pleural complications, of which 9.78 per cent were empyema, we reached 22.8 per cent with 5.2 per cent of empyemas; the number of pulmonary perforations was really trifling.

The more extensive use of intrapleural pneumolysis after 1940 also helped. During the period 1935-1940, 17 per cent of cases treated by pneumothorax had pneumolysis; while from 1941 to 1946 this was administered to 40 per cent.

The advent of antituberculosis drugs has resulted in remarkable changes in the treatment of tuberculosis, with different evaluation and employment of some methods of treatment.

The notion of gravity of a tuberculous process of the lung has been changing in the sense that instead of the criterion of extent of disease there has come the criterion of age. With recent lesions, there is a better expectation of recovery by treatment with antituberculosis drugs, independent of extent and location.

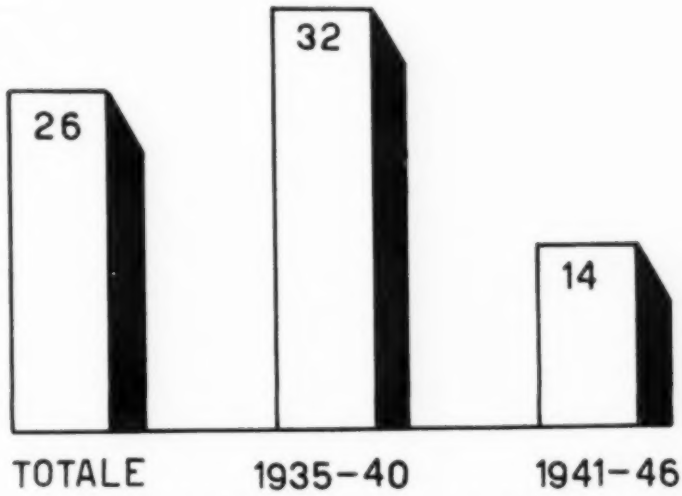

FIGURE 1: Total of deaths during treatment and after PNX suspension.

These new methods have influenced the use of intrapleural pneumothorax with reference to indications. In many cases it has been replaced by rest again considered suitable (following a period of unjustified unpopularity) by chemotherapy and resection. This was forecast by Forlanini in 1882 and could now be put into practice with the help of drugs either in the preparatory stage, with the regression of the most recent lesions, and by protecting against spread of the organisms following surgery. It was therefore unavoidable that intrapleural pneumothorax, dominating the treatment of pulmonary tuberculosis for almost a half century would receive a strong blow until it was almost completely abandoned in some countries of Europe and America.

A few authors not only pointed out the better and faster results of antituberculosis drugs and of resection associated with rest, but they also tried to disaffiirm everything that had been previously accomplished thus instituting a real protection against pneumothorax with a retroactive effect.

During this battle against pneumothorax some authors, especially North-

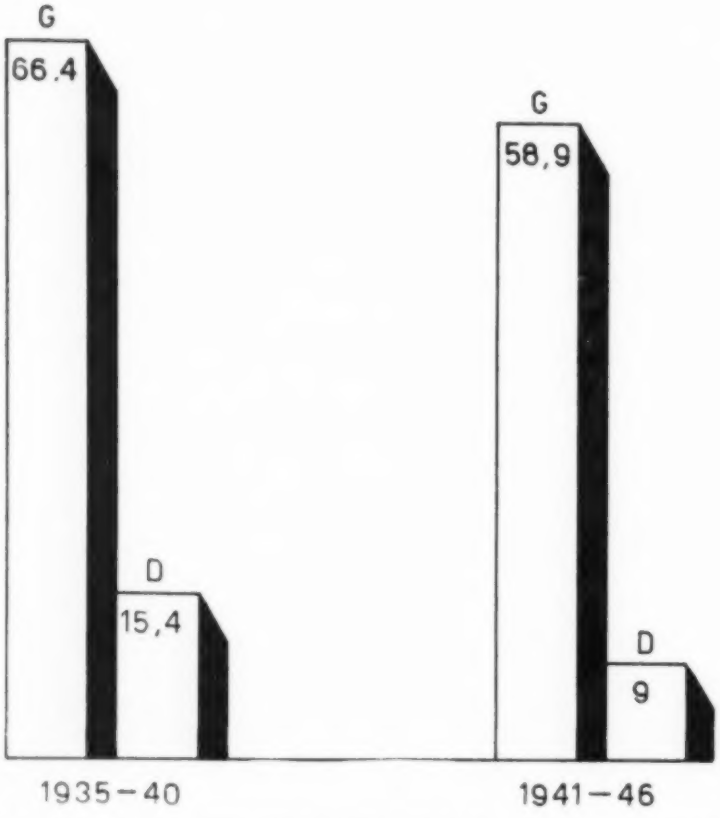

FIGURE 2: Patients recovered and patients dead after a minimum of 2 years from PNX suspension.

American and Dutch, stated that results of the method of Forlanini were not superior to those that may be attained only by sanatorium treatment, while the frequency and gravity of complications directly associated with pneumothorax, were, in their opinion, such that it had to be considered useless, or even harmful.

Is this disparaging propaganda justified nowadays? Does this therapeutic method have to be abandoned or has it still some value? We will try to give an objective answer to these questions, based upon our long experience and on the results of our investigations. We start by briefly analyzing the methods which have been proposed in the place of pneumothorax.

The advantages given by the antituberculous drugs in pulmonary tuberculosis are undeniable; when it is well carried out at least temporary recoveries have been observed without the use of other treatment. But it is also true that sometimes medical treatment alone is not sufficient to prevent the disease from becoming chronic without any additional therapeutic methods.

In addition to these failures of chemotherapy it has also to be remembered that there is the possibility of relapses, after a period of time, sometimes long, sometimes short, after treatment suspension.

The incidence of the new symptoms has been variously evaluated by different investigators, ranging from 34 to 36 per cent according to the statistics of Steinlin, Giobbe and Gaeta, to 6 per cent according to Et. Bernard. Recently Lucchesi, Zubiani and Catacchio on the basis of an accurate investigation of 551 patients, selected from among more than 5,000 who underwent rational and continued therapy, and were dismissed after recovery from the "C. Forlanini" Institute of Rome, revealed that relapses of 8.5 per cent were reduced to 5.8 per cent in patients treated at the same time by antituberculous drugs and intrapleural pneumothorax.

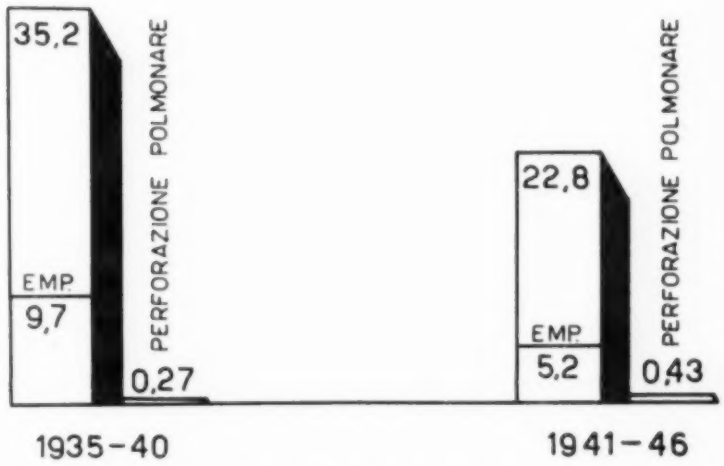

FIGURE 3: Main complications of PNX: pleuritis, empyema, perforation.

Pulmonary excision drew an undoubted advantage from improvement of surgical technique and anesthesia, and antituberculous drugs. But to state that following preparation by chemotherapy all patients still showing lesions can be efficaciously treated with single or multiple resections, is not to acknowledge that tuberculosis is a generalized disease and therefore cannot all be removed surgically.

Only some forms of post-primary tuberculosis (tuberculoma, cavities insufflated by bronchial stenosis, cavities of the lower lobes, tuberculosis associated with bronchiectasis, the cavity residuals after thoracoplasty, and so on), can constitute absolute indications for resection and they are just those for which, according to the experience of most of the workers in tuberculosis, intrapleural pneumothorax and others, collapse procedures are counterindicated.

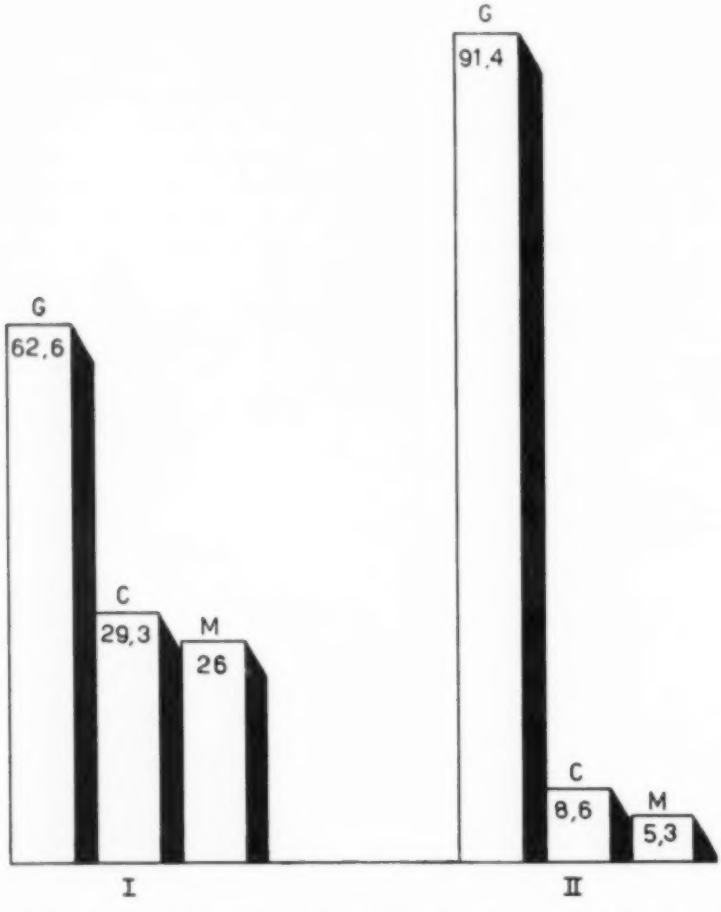

FIGURE 4: Results and complications of PNX in pulmonary tuberculosis for the periods: I (1935-46) without antibacterial therapy; and II (1947-53) with bacterial therapy. g = recovered; c = pleural complications (pleuritis, empyema, perforations); m = dead.

It is also important to appreciate the incidence of complications which may follow resection such as bronchial fistulae and empyemas.

Beaulieu, Whang and Duhaime reported that pleural fistulae following resection occurred in 13.5 per cent of cases.

As for the efficacy of the rest treatment we have to remember that it has been ratified since the second half of the past century. However this treatment is only a help and not a determinant means for clinical recovery from pulmonary tuberculosis.

The most effective argument in support of pneumothorax comes from the results of our statistical and clinical investigations. Between 1947 and 1953 we examined 569 cases with pneumothorax accompanied by chemotherapy (Figure 4).

The recoveries reached 91.4 per cent, deaths 5.3 per cent, complications 8.6 per cent (3 per cent with empyema and no cases of perforation). On the other side we reach 62.6 per cent, 29.3 per cent and 26 per cent (9.9 per cent with empyema and 0.9 per cent with perforations respectively) in cases with pneumothorax without chemotherapy.

Conclusions drawn from our investigations are as follows: Intrapleural pneumothorax having absolute indications has to be performed by a suitable technique, associated with antituberculosis drugs, completed with pneumolysis, yet represent a therapeutic method which only seldom causes complications, while it leads to a clinical recovery in a very high percentage of cases.

From what we have reported it seems that one of the most important arguments of the opponents of pneumothorax, pertains to complications, which are no longer significant.

If in the pre-antituberculosis drug era pneumothorax, notwithstanding a few dangers, represented, according to the general opinion, a valuable method, we do not understand why it is not to be performed nowadays, when its negative side has been practically eliminated. This statement is even more important, if we compare results and complications of pneumothorax with those of resections in pulmonary tuberculosis, both being accompanied by chemotherapy.

In Figure 5 on the left one sees percentage data collected by D. S. King on 3,840 patients treated with pulmonary resection which was preceded and followed by antituberculosis drugs in the Hospitals of the Veteran Administration in the years 1952-53-54. On the right the mean percentages of results and complications of pneumothorax combined with antituberculosis drugs are reported. They were collected from 1,200 patients within the years 1947-53 in the "C. Forlanini" Institute of Rome and from French authors Piechaud, Freour, Gestat and Urbain-Guinard. There is the same incidence of recovered patients, almost the same incidence of deaths. Pleural complications however are strikingly low for pneumothorax, while they remain comparatively high for resections, in spite of the large use of chemotherapy.

In order to complete a study concerning the therapeutic and social value of pneumothorax it seemed necessary to investigate the functional results of intrapleural pneumothorax at the end of treatment.

An investigation concerning pulmonary function at the end of the pneumothorax treatment has been made by Donno et al. They found that the vital capacity of the re-expanded lung represents, as an average, 41.1 per cent of the bronchospirometric amount instead of theoretical 48.4 per cent, while the whole value of effective C. V. compared with its theoretical value of 91.9 per cent. Analyzing each lung it is pointed out, in the re-expanded lung, that C. V. is reduced on an average of 79 per cent of its theoretical value, with a minimum of 55.6 per cent and a maximum of 103 per cent. On the contrary, the small consumption of oxygen by the re-expanded lung was reduced on an average of 57.5 per cent of its theoretical value. These investigations were made on 10 patients who had ended pneumothorax after two years of treatment.

The data drawn from our study of the cases show the great improvement in pulmonary function obtained by careful choice of cases to be treated by simultaneous use of drugs.

For a better explanation we have subdivided the results collected by the tests of Knipping-Scoz and sometimes of separated bronchospirometry

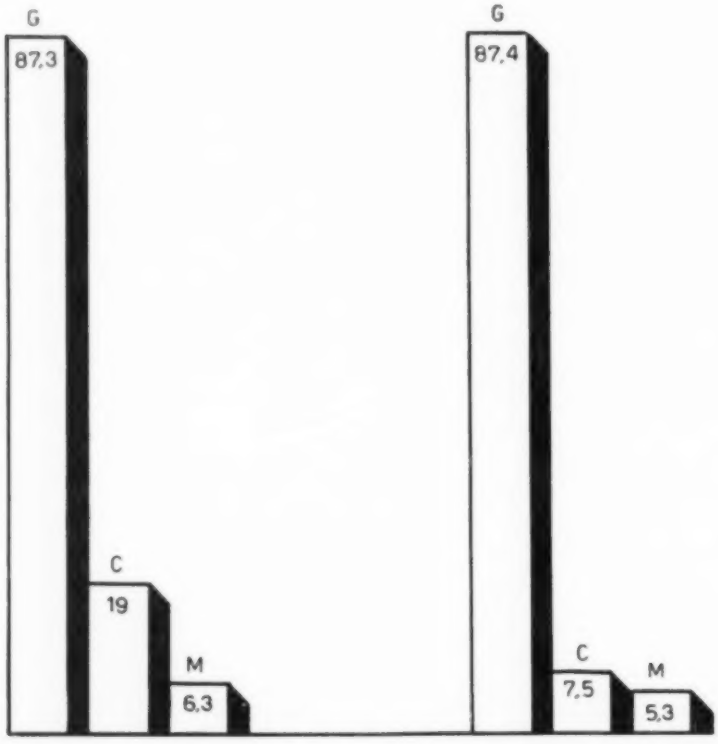

FIGURE 5: Results and complications of resections and PNX combined with antibacterial therapy according to King (Veteran Administration Hospitals) and according Fegiz, Piechaud, Freour, Gestat, Urbain-Guinard. Left side of the table: Means of 3,840 cases (from 1952 to 1954) treated with resections. Right side = mean of 1,200 cases (from 1947 to 1953) treated with PNX. g = recovered: c = pleural complications (fistulae, empyemas) m = dead.

into: good, middle and bad results. In the first group the respiratory function tests yielded nearly normal results or modest changes well counterbalanced and whose working capacities has to be considered almost normal.

In the second group we have included the subjects whose tests showed a deficiency, mainly following exertion. The deficiency was generally counterbalanced by less excessive and protracted exertion so working capacity was confined to lighter works.

In the third group are subjects with considerable deficiency and minimal ability of compensation, and a working capacity nearly nil.

As shown by the sixth graph Figure 6 before chemotherapy, there had been, in the years from 1940 to 1946, improvement of the patients with a good respiratory function at the end of treatment. These patients have shown a sudden increase after introduction of antituberculosis drugs with pneumothorax, reaching only 5.5 per cent with bad pulmonary function.

Replying to our two previous questions we can at last come to the conclusion that artificial pneumothorax nowadays has an important role in the treatment of pulmonary tuberculosis in addition to antituberculosis drugs and in addition to the surgical resection. Therefore the criticisms by some authors are unjustified.

Omodei Zorini, on the occasion of the Congress of Internal Medicine held in Rome, 1947, uttered a caution which still holds with regard to the objective evaluation of the new medications: "the antibacterial therapy

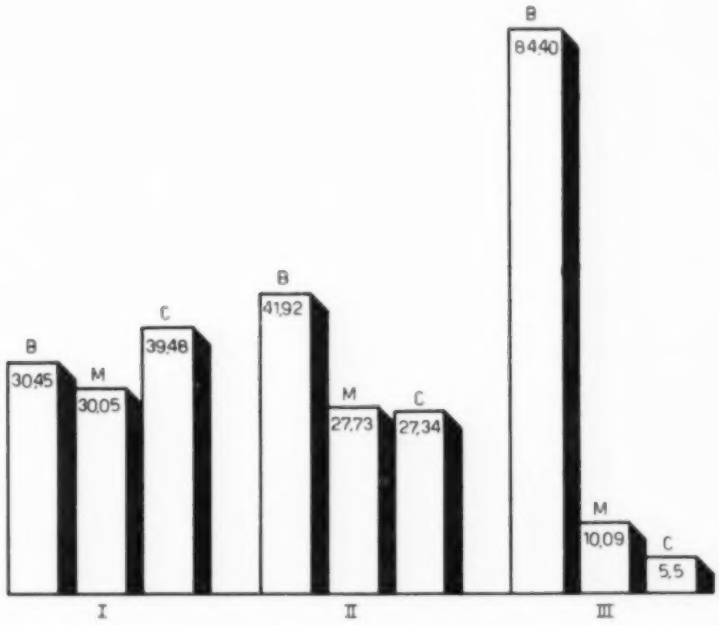

FIGURE 6: Pulmonary function by the end of the pneumothoracic treatment for the periods: I (1935-40); II (1941-46); III (1947-53) B/good; M = modest C = bad.

cannot still replace artificial pneumothorax, but, on the contrary, pneumothorax is often combined with the above mentioned therapy, allowing, in such a way, the institution of an effective collapse in some cases where the collapse therapy would have been impracticable at the beginning and dangerous; if therefore pneumothorax has lost, in part, its importance in some fields, it could gain in other fields, by its extension to patients on whom it was not feasible before." He still states that "the divergency of the conception and of training about the treatment of tertiary pulmonary tuberculosis is determined by the prevalence of the surgeons on the clinical Doctors in some phthisiologic centers, mainly Anglo-Saxon. For the above mentioned reason the task of the latter is reduced in practice to the simple role of preparing in the best way the patient to the surgical operation, when the patient does not recover by medical treatment alone. . . ."

From our paper, the benefits following antituberculosis drugs in pneumothorax treatment are self-evident, either considering them on clinical or on economical and social grounds. Recoveries reached by such a combination are safer and more effective, having a percentage of relapses remarkably lower than those obtained by drug treatment alone (see data collected by Lucchesi and his co-workers). It is so possible to avoid chronicity which represents a heavy damage not only economically but also socially speaking. These patients still represent a serious source of infection and they are therefore an obstacle for the regression of morbidity caused by tuberculosis especially because they are often treated ambulatorily.

Also in comparison with pulmonary resection pneumothorax combined with chemotherapy has some advantages, as far as we are concerned.

It is not an exception to find surgically operated patients, who became invalid either because of marked functional deficiencies, more numerous than those caused by pneumothorax, or because of bronchial fistulae with resulting empyema.

At the end of this paper, we think it to be advisable to expose the present orientation of our School with regard to pneumothorax. They can be synthetized as follows:

1. *Preparatory antituberculosis drug treatment.* It is a serious mistake to begin pneumothorax for recent exudative disease, without having previous preparation based on rest and antituberculous drug treatment, not to exceed two or three months. The clinician is most qualified to decide whether pneumothorax should be instituted and the best time for it to be started. He is aided by clinical, radiological and biological investigations. Collapse therapy should be started before cavitation begins to stabilize and become chronic. However it has to be delayed or not considered at all, if one is sure that the lesions are being well controlled by simple drug treatment. Over delay, on the contrary, in case of initial chronicisation, can cause inefficiency of collapse therapy because of thickening of the walls of the cavity due to fibrosis.

Therefore, we do not agree with opinions of some authors on "delayed pneumothorax," namely pneumothorax delayed for some months and sometimes for one or two years, during which the patient is subjected to absolute rest and intensive antituberculosis drug therapy.

2. *Indications.* By absolute indications we mean cases moderately advanced, renilateral exudative or miliary tuberculosis, mainly of one or two lobes, with cavities of the maximum diameter of 3 cm. and placed in easily collapsible sites.

Relative indications are given by tuberculous phthysiogenic processes, concerned with the upper half of the lungs, especially if there is a clear disproportion of extent of disease in the two lungs. These cases cannot generally be treated by resection having previously received surgical treatment on one side (namely thoracoplasty, extrapleural pneumothorax, pulmonary resection).

It is obvious that one should also exclude cases of cirrhotic tuberculosis, fibrosis, thickening over the apexes, bronchoasthmatic or emphysematous tuberculosis, tuberculosis of aged people, too extensive bilateral forms, the old thick walled cavities, isolated cavities at the pulmonary bases, lesions associated with bronchiectasis or pulmonary abscesses.

3. *Complementary treatment.* At the beginning, during or after pneumothorax antituberculosis drug therapy has to be administered for at least two or three months. These have to be alternated with periods of rest in order to facilitate the biological recovery from tuberculosis and to avoid complications.

4. *Behavior of the treatment.* Treatment has to be carried out with rather short refills intervals (the best is weekly refills), only enough air should be used to insure good collapse of the lung and for cavity closure. In the event of pleural complications, in addition to pneumothoracentesis, according to C. Forlanini and E. Morelli, one may administer intrapleurally a cortisone agent simultaneously with antituberculosis drugs but maintaining pneumothorax. If fluid continues to form or show a tendency to convert to empyema, one may abandon pneumothorax and perform a pleuropulmonary decortication. The same treatment has to be used in the case of thickening of the visceral pleura.

5. *Duration of the collapse.* At present, one tends not to exceed two or three years of treatment. Special care has to be observed at the time of discontinuing pneumothorax to avoid pleural effusion *ex vacuo* which could lead to hooped and unexpandible lung. In order to prevent possible late empyemas and pulmonary perforations, such effusions have to be systematically evacuated. Discontinuation of pneumothorax has to be gradual and simultaneous with chemotherapy for four to six months.

We agree with the great scientist E. Rist who in 1954 said, "It is possible, I believe, to predict without the risk of being led from the facts, that there will always be tuberculous patients for whom pneumothorax associated or not with antibiotics, will be the safer and lasting way to the recovery."

Pneumoperitoneum (PNP)

In Italy this method did not enjoy the same favor as in other countries. In the United States of America (where the method was conceived and used by Banyai) pneumoperitoneum was much used in sanatoria at least until a few years ago. According to Bobrowitz, (1953), from 1947 to 1951, the number of cases of pneumoperitoneum started at a sanatorium in New York City, charged from 25 in 1947 to 175 in 1950, and de-

creased to 135 in 1951. At the same time, the number of refills rose from 543 in 1947 to 9,568 in 1951. Crenshaw and Gross, Battey State Hospital, Rome, Georgia, administered about 25,000 in 1953, which corresponds by a rough calculation to 700 patients treated with pneumoperitoneum.

It seems that in the Eastern Countries, pneumothorax is extensively used for patients with pulmonary tuberculosis, according to the papers of Garbinski, Pregowski and Szwanke at the last Polish Congress of Phthysiology.

In Italy there are statistics concerning pneumoperitoneum either as a collaspe therapy method, or applied in association with the paralysis of the diaphragm (Fegiz, Rabino, D'Ambrosio, Bortolotti-Boffo).

At the Forlanini Institute, pneumoperitoneum is considered as a method of collapse therapy definitely less effective than intrapleural pneumothorax. However less complications occurred—pneumoperitoneum.

Presently this superiority of pneumoperitoneum does not exist because the simultaneous use of drugs and pneumothorax has greatly lowered pleural complications. For this reason, and from all standpoints, the method is much better than pneumoperitoneum.

Actually, in our Institute, in a total of 1,380 patients with pulmonary tuberculosis, 224 received intrapleural pneumothorax and 43 pneumoperitoneum, a proportion 1:5 with pneumothorax and 3.1 per cent of all patients.

It is best to start pneumoperitoneum following suitable preparation by rest and antituberculosis drugs. The preparatory time fixed by us is two months for pneumothorax and three to four for pneumoperitoneum.

Our present indication for pneumoperitoneum are:

1. Pneumoperitoneum combined with antituberculosis drugs in bilateral widespread nodular forms, mainly in those with extension beyond the middle pulmonary field, the basal bronchopneumonic type, being mono or bilateral generally following hemoptysis, and finally ulcerous lesions of the lower lobes.

2. Pneumoperitoneum associated with intra and extrapleural pneumothorax. Pneumoperitoneum is indicated when because of symphisis of the bases, the collapse is not adequate to control the lesions, or because of secondary effusions in the area. Also the "cord-pneumothorax," as Omodei-Zorini has reported several years ago, can be a favorable indication for pneumoperitoneum, which, in such a way, replace phrenicoexeresis.

3. Pneumoperitoneum associated with thoracoplasty and resection in pulmonary tuberculosis. The present indications for pneumoperitoneum in association with thoracoplasty are essentially the same of those described for the gaseous intra and extrapleural collapse therapy.

With this method, it is possible to prevent the post-surgical spread in the lower lobes and even more, it can facilitate regression once they appear. It seems that especially in these cases pneumoperitoneum has a peculiar power hastening and accomplishing dissolution of the bronchopneumonic foci.

Association of pneumoperitoneum with resection we think is very useful after lobectomies, mainly lower, and after segmental resections in

order to facilitate the normalization of the chest cavity and in order to prevent overdistension and residual lobes, especially if there are apparent latent foci.

Pneumoperitoneum applied with these criteria, in about 20 years of experience, has given us very satisfactory results, especially considering the simplicity of the method and its usual better tolerance.

The most favorable results, can however be observed in mediothoracic lesions, where an attempt at pneumoperitoneum has to be done before entrusting a patient to the surgeon for resection. In a few cases, in fact, the efficacy of pneumoperitoneum has been so rapid and complete as to make intervention of the surgeon unnecessary. Pneumoperitoneum is then a most valuable complementary method of treatment.

SUMMARY

With the aim of making clear the present situation of pneumothorax in the treatment of pulmonary tuberculosis, we have analyzed 1,762 cases treated between 1935 and 1953 at the "Forlanini" Institute of Rome, and followed for at least two years after the treatment was discontinued.

Before the advent of antituberculosis drugs in the years 1935-46, the mortality rate was 26 per cent, recoveries of 62.5 per cent, complications 29.6 per cent (of which 9.9 per cent were empyemas).

Lately, with the addition of drugs deaths decreased to 5.3 per cent, recoveries increased to 91.4 per cent, and complications fell to 8.6 per cent (of which 3.8 per cent were empyemas).

Compared with data collected by King on 3,840 patients with pulmonary resection and antituberculosis drugs, mortality and recovery rates were about the same as those with pneumothorax. Pleural complications were higher for the operated patients (18 per cent).

Pulmonary function has also been less impaired since the introduction of chemotherapy. Among our patients good pulmonary function following treatment was 30.5 per cent (1935-40) 41 per cent (1941-46), and 84 per cent (1947-53). Intrapleural pneumothorax combined with antituberculosis drugs has a good position today in the treatment of pulmonary tuberculosis. Pneumoperitoneum has good possibilities as a complementary method in the medical and surgical treatment of pulmonary tuberculosis, but it gives results clearly inferior to those obtained with pneumothorax.

RESUMEN

Con el objeto de aclarar la posición actual del neumotórax en el tratamiento de la tuberculosis, hemos analizado 1762 casos tratados entre 1935 y 1953 en el Instituto Forlanini de Roma y seguidos por lo menos durante dos años después de la interrupción del tratamiento.

Antes del advenimiento de las drogas antituberculosas, en los años de 1935 a 1946, la mortalidad fué de 26 por ciento y las recuperaciones de 62.5 por ciento; las complicaciones 29.6 por ciento de éstas 9.9 por ciento fueron empiemas).

Más tarde con la adición de las drogas, las defunciones cayeron a 5.3 por ciento, las recuperaciones llegaron a 91.4 por ciento y las complicaciones sólo 8.6 por ciento (de éstas 3.8 por ciento fueron empiemas).

Comparados con los datos reunidos por King en 3.840 enfermos con resección pulmonar y drogas antituberculosas, la mortalidad y las recuperaciones fueron aproximadamente las mismas que con el neumotórax. Las complicaciones pleurales son mós elevadas en los operados (18 por ciento).

La función pulmonar fué también menos dañada desde la introducción de la quimioterapia. Entre nuestros enfermos se obtuvo una buean función pulmonar después del tratamiento en 30.5 por ciento (1935-40); 40 por ciento (1941-46) y 84 por ciento (1947-53). El neumotórax intrapleural combinado con las drogas antituberculosas tiene una buena posición hoy en el tratamiento de la tuberculosis. El neumoperitoneo tiene buenas posibilidades como método complementario en el tratamiento médico y quirúrgico de la tuberculosis pulmonar, pero claramente da inferiores resultados a los proporcionados por el neumotórax.

RESUME

Dans le dessein de clarifier la situation actuelle du pneumothorax dans le traitement de la tuberculosè pulmonaire, nous avons analysé 1762 cas traités entre 1935 et 1953 à l'Institut Forlanini de Rome, et nous les avons suivis pendant au moins deux années après que le traitement ait été cessé.

Avant l'apparition des médications antituberculeuses, le taux de mortalité dans les années de 1935 à 1946 fut de 26%, les guérisons de 62,5%, les complications 29,6% (parmi lesquelles 9,9% d'épanchements).

Dernièrement, avec l'association des médications, les décès ont diminué jusqu'à 5,3%, les guérisons ont augmenté jusqu'à 91,4% et les complications sont tombées à 8,6% (parmi lesquelles 3,8% d'épanchements).

Comparées aux données recueillies par King sur 3.840 malades ayant subi une résection pulmonaire associée aux médications antituberculeuses, les taux de mortalité et de guérison sont sensiblement les mêmes que ceux du pneumothorax. Les complications pleurales furent plus élevées pour les malades opérés (18%).

La fonction pulmonaire a aussi été moins lésée depuis l'introduction de la chimiothérapie. Parmi nos malades, ceux qui avaient une bonne fonction pulmonaire après traitement représentaient 30,5% de 1935 à 1940, 41% de 1941 à 1946, et 84% de 1947 à 1953. Le pneumothorax intrapleural associé aux médications antituberculeuses est en bonne position aujourd'hui dans le traitement de la tuberculose pulmonaire. Le pneumo-péritoine offre de bonnes possibilités comme méthode de complément dans le traitement médical et chirurgical de la tuberculose pulmonaire, mais il donne des résultats nettement inférieurs à ceux obtenus par le pneumothorax.

ZUSAMMENFASSUNG

Mit dem Ziel, die gegenwärtige Lage des Pneumothorax bei der Behandlung der Tuberkulose zu klären, haben wir 1762 Fälle analysiert, die zwischen 1935-1953 am "Forlanini-Institut" in Rom behandelt und mindestens 2 Jahre weiter verfolgt worden waren, nachdem die Behandlung aufgehört hatte.

Vor der Bereitstellung antituberkulöser Heilmittel in den Jahren 1935-

1946 betrug die Mortalität 26%, die Zahl der Wiederherstelleungen 62,5% der Komplikationen 29,6% (von denen 9.9% Empyeme waren).

Später nach Hinzufügung der antibyotica fiel die Zahl der Todesfälle auf 5,3%, diejenige der Wiederherstellungen erhöhte sich auf 91,4% und diejenige der Komplikationen fiel auf 8,6 % (von denen 3,8% Empyeme Waren).

Im Vergleich mit den von King zusammengestellten Zahlen von 3840 Kranken mit Lungenresektion und antituberkulösen Heilmitteln lagen Sterblichkeit und Wiederherstellung ungefähr in der gleichen Höhe mit dem Pneumothorax. Die pleuralen Komplikationen für die operierten Kranken waren höher (18%).

Die Lungenfunktion wurde ebenfalls weniger beeinträchtigt seit der Einführung der Chemotherapie. Bei unseren Krankenbetrug die Zahl der guten Lungenfunktionen nach Behandlung 30,5% (1935-1940); 41% (1941-1946); und 84% (1947-1953). Der intrapleurale Pneumothorax kombiniert mit antituberkulösen Heilmitteln besitzt heute eine gute Stellung für die Behandlung der Lungentuberkulose. Das Pneumoperitoneum verfügt über gute Möglichkeiten als eine ergänzende Methode der internen und chirurgischen Behandlung der Lungentuberculose, aber seine Resultate liegen deutlich unter denjenigen, die mit Pneumothorax erreicht werden.

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Pulmonary Cystic Disease: Observations in Cases Treated by Exploratory Thoracotomy*

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Introduction

Cyst formation in the lungs is gaining prominence as a topic of discussion in the current literature on respiratory diseases. Interest in this abnormality evolved from the observations in the phenomenon of spontaneous pneumothorax. Prior to 1932 the latter was universally considered as due to tuberculosis. In that year, however, Kjaergaard[1] submitted evidence to the contrary pointing out that patients with spontaneous pneumothorax had no more tuberculosis than was found in the general population. For this reason he proposed the term "pneumothorax simplex." This pioneer observation was fruitful since it became apparent that spontaneous pneumothorax is due to a peculiar abnormality in the lung rather than infection. Kjaergaard[1] postulated that the mechanism responsible for the phenomenon was rupture of an emphysematous bleb or bulla. This thesis has been amply confirmed by subsequent investigators.

Published reports on cystic disease discuss more commonly observations on cysts of bronchial origin. An increasing literature on the subject indicates, however, that emphysematous blebs and bullae of alveolar origin occur more frequently. In reports on bullous emphysema the occurrence of spontaneous pneumothorax is a commonly described symptom complex, and the procedure of underwater seal catheter decompression of the collapsed lung is stated to be a successful therapeutic measure in obtaining lung expansion. The utilization of exploratory thoracotomy for the purpose of carrying out excision of the cystic areas with the view of preventing the recurrence of spontaneous pneumothorax is not adequately stressed. Similarly, occurrence of infection within the cyst and hemoptysis likely caused by a sudden increase in pressure within it are not described frequently nor are these complications generally known. Clinical investigators of this subject have posed a number of inquiries, such as: Their congenital or acquired origin; whether antecedent respiratory infection may be contributory to their development; whether generalized emphysema accompanies localized cystic degeneration confined to a lobe or segment of a lobe; and whether a correlation exists between the severity of symptoms and the number and size of the cysts. The type of cystic disease this paper is concerned with is the developmental variety. It is characterized by progressive destruction of the interalveolar septa within a lung segment. This leads to bulla or cyst development and ensuing compression of contiguous lung parenchyma.

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Material and Methods

The present study concerns a group of 21 cases of cystic disease confirmed by exploratory thoracotomy which was performed in service hospitals, private institutions and facilities of the Veterans Administration. Observations were made with reference to symptomatology, roentgenological abnormalities, history of respiratory infection, incidence of cyst infection, occurrence of hemoptysis and spontaneous pneumothorax, surgical findings, operative procedures and the histopathological pattern of the resected specimens. In evaluating the components of the total picture of cystic disease a striking feature of this study is the high incidence of roentgenological abnormalities that obscured the true nature of the underlying pathology confirmed at the time of exploratory thoracotomy.

Analysis of Material

The incidence of symptoms was classified in the following categories: 1) Constantly present (11 cases), 2) Intermittently present (eight cases), 3) No symptoms (two cases).

In group 1, symptoms were continuous and over a period of many years. In group 2, symptoms appeared either when spontaneous pneumothorax developed or when the cyst became infected. In group 3, there were no symptoms at any time; the diagnosis of cystic disease was made on "routine" x-ray film examination. In only eight cases was cough present. Sputum was present in seven; in four it was mucoid in character and the amount varied between three and four ounces. In three it was purulent and resulted from cyst infection. In the latter, the preoperative diagnoses were probable lung abscess, infected cyst or tuberculous cavity. Dyspnea was presented in 12; it was constant in only six; in the other six cases it occurred only during an episode of spontaneous pneumothorax. Hemoptysis occurred in four cases; in two of these the preoperative diagnosis rested between abscess, tumor, or infected cyst. In the other two cystic pathology was unmistakable by x-ray films. Spontaneous pneumothorax occurred in six. In five it was unilateral and in one it was alternating. In two it occurred three times; in one six times; in one 9 times; in one patient experienced 30 episodes of lung collapse. Two had fever and

TABLE I

Symptoms Noted		Case Incidence
Cough		8
Sputum	Mucoid - - - - - - - - - - - - 4	7
	Purulent - - - - - - - - - - - 3	
Chest Pain		9
Dyspnea		12
Hemoptysis		4
Spontaneous Pneumothorax		6
Fever		2
Weight Loss		2
Chest Colds		2
Wheezing		1
Congestive Failure		1
Difficulty in Swallowing		1

TABLE II—X-RAY FINDINGS

X-Ray Signs Resembling Other Pathology	Number of Cases	X-Ray Signs Consistent With Cystic Disease
Fibrosis Right Middle and Lower Lobes	1	9 Cases
Lung Abscess	3	
Lung Tumor	3	
Mediastinal Tumor	1	
Tuberculosis	1	
Mediastinal Lymphadenopathy	1	
Arterio-Venous Fistula	1	
Congestive Failure	1	
TOTAL	12	

were found to have cyst infection. In the two that sustained weight loss, one had cyst infection accompanied by fever, purulent expectoration, prostration, and anorexia; in the other, the cyst was situated within the mediastinum, exerting pressure upon the esophagus making swallowing difficult to the extent that food intake was diminished. A history of respiratory infection was obtained in two and these did not present any striking association with the cystic disease in a cause-and-effect relationship. Wheezing occurred in one and could be attributed to the presence of bronchospasm. One presented symptoms and signs of congestive failure.

The roentgenological signs previously alluded to are intriguing since more than half of the group showed abnormalities that simulated pathology other than cystic disease.

Table II is self-explanatory but certain points should be stressed. A pyogenic infection within the cyst or blocking the egress of secreted mucus from the cyst can make for an erroneous diagnosis of abscess in the first instance and tumor in the second. Again, when a cyst is situated within the mediastinum it can be mistaken for tumor or lymphadenopathy.

FIGURE 1

FIGURE 2

Figure 1: 1949—Note small cysts on right and large cyst on the left.—*Figure 2:* Cyst showing blocking of respiratory bronchus. Note fluid level (same case 1954).

It is especially noteworthy that cyst infection occurred in seven cases and resembled acute or chronic bronchopulmonary suppuration or frank pyogenic lung abscess. In one a zone of fibrosis was a masking abnormality. In another the probability of a tuberculous cavity with a blocked draining bronchus and a fluid level within it was considered. In another instance a mediastinal cyst was interpreted as due to mediastinal lymphadenopathy. One resembled an arterio-venous fistula in an upper lobe. Exploratory thoracotomy proved it to be a "cystic reduplication" of a branch of the main stem bronchus. Lastly, one simulated congestive failure. No concomitant diffuse, hypertrophic, pulmonary emphysema was encountered in the series herein reported.

Of further interest is the anatomical localization of the cysts. Reports on cystic disease stress that their common location is in the apex or upper lobe. In the group reported herein, except for four that were situated within the mediastinum, they were equally distributed within the lower as well as the upper lobes of the lung. The chart below is illustrative of their localization.

Operative findings in the group of cases herein reported are of considerable interest. The cysts were large and small, single or multiple, pinhead or giant size. A large cyst, sometimes referred to as "giant bulla," is able to compress a large portion of the lung thus depriving it of ventilatory function. This occurred in two instances. The effect of infection within a cyst was noted in one case in which necrosis of its wall so extended the infection that a fistulous tract was established between the cyst and the subdiaphragmatic structures adjacent to the lower lobe where the cyst was located. In one there was a clear-cut developmental anomaly characterized by a cystic reduplication of a branch of the main-stem bronchus. One consisted of a cystic mass within which were found solid concretions of mucus. One presented universal air leakage from the entire lung surface when positive intratracheal pressure was induced by the anesthetist. It can be postulated that the air leakage described was due to the following pneumodynamics: First, a ball-valve mechanism in the main stem bronchus permitted air to enter the cysts and none was able to escape. This created a progressive increase in intracystic pressure.

TABLE III
SITE OF CYSTS—LOBAR DISTRIBUTION

Location	Case Incidence
Right upper lobe	4
Involving both right upper and middle lobes	1
Right middle lobe	2
Involving both right middle and lower lobes	1
Right lower lobe	3
Left upper lobe	2
Lingula, left upper	1
Left lower lobe	3
TOTAL	17
Within the mediastinum	4

Second, the cyst wall was so thinned out that it developed the attributes of a permeable membrane. Such observations have been reported by Sattler.[2] The latter has shown in his investigations on spontaneuos pneumothorax phenomena that when the bronchial block mechanism is eliminated, air leakage through the wall of a lung cyst ceases spontaneously.

As regards the operative procedures utilized in the treatment of the cases described in this paper, the following techniques were employed: In some cases primary underwater seal decompression was used preparatory to exploration. At a later date the cyst was excised en masse when it was technically feasible. In other instances when fusion existed between the cyst and adjacent structures, it was first opened and was followed by excision. A common procedure employed after cyst excision was either imbrication or plication of the cyst bed. When the cyst was an integral part of a lobar segment or an entire lobe, a segmental lobectomy or total lobectomy was performed. Here, too, the operative bed was sewn over by plication. Lastly, when minute blebs were encountered adjacent to the site of excision, simple puncture and air evacuation from these accompanied by a sewing over technique was the common procedure. In the group under discussion the following procedures were employed: Six cases were treated by segmental lobectomy; four had lobectomy; cyst excision alone was performed in 10; one that presented two cysts had a pleurectomy and partial decortication with plication performed after the cysts were opened. In another case, presenting a single cyst which was excised, a neighboring zone of minute emphysematous blebs was treated by pleural "irritation" with the view of establishing pleural inflammation and ensuing symphysis in an effort to prevent the recurrence of spontaneous pneumothorax that the patient had experienced previously. The procedure of pleural "irritation" has in recent years replaced the former practice of pleural "poudrage" which utilized iodized talcum powder.[3] While the latter procedure was frequently effective it was often accompanied by severe pain and has been abandoned almost universally in recent years.

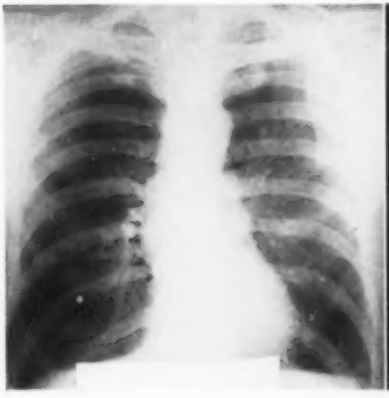

FIGURE 3

FIGURE 4

Figure 3: 1946—Note lobulated mass in right hilus region, resembling neoplasm.—*Figure 4:* Same case, lateral view, large cyst is seen. It was resected.

The histopathological findings in cystic disease are variable. When metaplasia occurs, its normal lining may be replaced by squamous epithelium or, when the cyst has become infected, the normal epithelium may be completely destroyed and replaced by fibrosis. The latter type of tissue can be the cause of bleeding which this writer desires to designate as "spontaneous hemorrhage." Other types of tissue found to line a cyst are columnar ciliated epithelium and cuboidal epithelium. Of special interest is the presence of trabeculation consisting of fibrous bands extending from one portion of the cyst lumen to another, usually arranged in a vertical manner. When noted on the x-ray film they should arouse suspicion of the presence of cystic disease. Two of the cases showed varying degrees of trabeculation which was a notable component of a diffuse fibroplasia occupying the entire cyst membrane. Only one case gave indication of congenital origin; it had cystic reduplication of a bronchus with infection within the reduplicated bronchial channel. The preoperative diagnosis was arteriovenous fistula.

Discussion

Knowledge concerning cystic disease of the lungs dates to Thomas Bartholinus who in 1687 described its anatomy.[4] In 1925 Koontz[5] collected 108 cases from the literature. In 1936 Schenck[6] reported on 381 cases that had appeared in the literature up to that year. According to Brantigan[7] 400 papers were published on this subject during the period 1939-1949. Probably reports on cystic disease will increase as exploratory thoracotomy is more widely used in the treatment of recurring spontaneous pneumothorax or in the management of the cases that present progressive dyspnea associated with cyst formation that is accompanied by compression of normal lung parenchyma.

Cystic disease has been described variously as "air-cell," "cystic emphysema," "air cyst," "giant bulla," "emphysematous bleb," "bullous emphysema," "pneumotocele," "broncho alveolar cyst," "alveolar cyst," etc. They are classified into two anatomical types, bronchial cyst and alveolar cyst. The former is considered congenital in origin; the latter, acquired. Another classification refers to the mode of localization, such as cyst formation within a lobe designated as localized emphysema, and a second

FIGURE 5: Another case showing cyst, shaped like a globe.

type, the generalized type in which bullae and blebs are part of a diffuse bilateral hypertrophic emphysematous process. This paper deals with the localized type of cystic disease.

Several hypotheses have been advanced to explain the mechanism of cyst formation. One is the mechanical theory in which the following events are described: Due to stenosis, distortion or occlusion of a segmental or lobar bronchus supplying a particular portion of the lung, ingress of air takes place into the corresponding lung segment but cannot make egress because of the development of a ball-valve mechanism. This leads to an ever-increasing pressure build-up within the lung segment, resulting in a thinning out of the alveolar septa. The latter eventually desintegrate and an air cyst is formed. This theory is given considerable support by the anatomical studies of Hayashi[8] and Miller.[9] The latter have noted that pulmonary cysts are generaliy connected with bronchiales or respiratory bronchiales. Furthermore, the latter have observed the presence of valve-like structures within these bronchiolar ducts. Another hypothesis of causation considers a vasculo nutrient factor involving the blood vessels that nourish the alveolar septa.[10] According to this theory diminution of blood causes disintegration of the alveolar wall. According to Cudkowicz[11] (quoted by Alarcon[12]) cyst formation results from a lack of blood supply to the alveolar septa because the bronchial arteries are in a state of spasm. If the theory just described is tenable, the "loss of life" in the alveolar septa can be attributed to a process of "aseptic necrosis" making for alveolar disintegration, alveolar coalescence and finally formation of air cysts. A parallel phenomenon of cyst formation is noted in cases of anthracosilicosis. Here, too, air cysts are found, and the theory of their production is similarly considered as due to interalveolar septum necrosis due to shutting off the blood supply to a lung segment because of bronchial artery blocking by silicon particles.[13] It can be speculated that early in the process the vascular effect might be reversible. This has been stressed by Alarcon in his observations on lung cysts seen in the evolution of tuberculous pathology. Thus, with a return of the circulation bullae might disappear. In discussing the reversibility of cyst formation Alarcon[12] speculates that tuberculotoxins might be responsible for the disintegration of the alveolar septum. The reversibility of bullae has been observed by others.[14]

Symptomatology in cystic disease is variable, and depends upon several factors: If the cyst is large enough to compress contiguous lung parenchyma, dyspnea is the outstanding symptom. If normally functioning lung is not compressed, the patient may have numerous cysts even bilaterally and present little if any respiratory distress. If infection occurs within it symptoms of an acute pyogenic abscess supervene. If intracystic pressure is sufficiently great, the vascular components within the cyst wall can rupture; or if the vascular channels are particularly abundant as the result of conversion from normal columnar or metaplastic squamous epithelium to fibrous tissue, blood vessels can rupture easily producing hemoptysis varying in degree from blood streaks to frank hemorrhage. Finally, an outstanding event of variable magnitude may take place when a spontaneous pneumothorax supervenes due to the rupture of a thinned out cyst wall. In this instance, if the perforation does not seal over, the development of a tension pneumothorax is an ever present danger. Cardiopulmonary failure can be so severe that unless immediate and energetic measures of pleural decompression are carried out promptly, life itself may be threatened. Generally, the

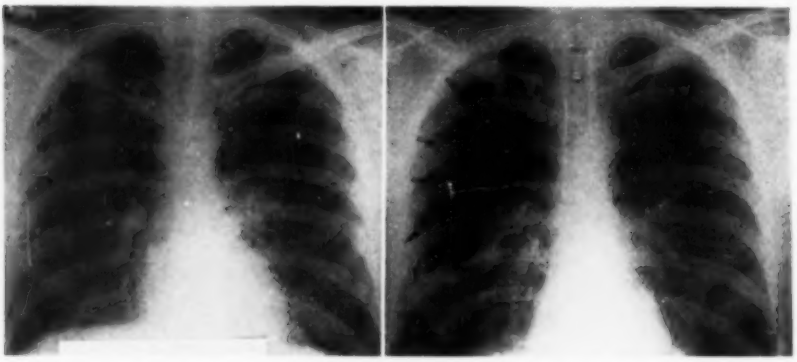

FIGURE 6 FIGURE 7

Figure 6: October 15, 1945. Arrows point to absence of bronchovascular markings in both apexes characteristic of cystic disease.—*Figure 7:* February 18, 1953. Same case, years later. Note progression of pathology; arrows point to large areas of avascularity in the upper ⅔ of the right lung and upper portion of left upper lobe. Note compression of right lower lung field.

symptoms that may be annoying over a long period are paroxysms of cough accompanied by mucoid expectoration, but as already indicated these symptoms are often times not in evidence.

Recognition of cystic disease on the roentgenograph may be relatively easy or extremely difficult. Very small emphysematous bullae or blebs may not be recognized at all. In several reported series in which exploratory thoracotomy was performed to forestall future episodes of spontaneous pneumothorax, no abnormalities were seen in 91 per cent of preoperative films. The general characteristics of cystic disease are ill-defined zones of increased radiance in some portion or portions of the lung; diminution and sometimes complete absence of the bronchovascular markings, the so-called "phantom lung" pattern;[15] or a thin wall structure that encompasses an area of increased radiance, the so-called air cyst. Moreover, in cystic areas in which considerable pressure build-up has occurred, a guide to the basic pathology will be found in the compressed portion of the lung lying in apposition to the cystic area. Under these circumstances the compressed portion of the lung may be erroneously interpreted as a zone of localized fibrosis. Actually it is an anatomic variation resulting from compression by a neighboring cyst. Another phenomenon that is a helpful guide in the localization of lung cysts is the recognition of linear bands of density within a zone of increased lung radiance. They are called "trabecules" and are the shadows produced by fibrous bands that frequently traverse air cysts. They usually arrange themselves in a vertical manner. Further, regarding the difficulty in recognizing the small bullae or blebs that have precipitated episodes of spontaneous pneumothorax by their rupture, Shefts et al.[16] report that in their observation of such cases they are able to detect the blebs or bullae more readily during the early phases of lung expansion.

In the group of cases herein presented a known episode of infection that could possibly be considered as a related factor to the presence of the cystic pathology was considered in two cases. However, it is not certain that these cases were entirely free from pulmonary pathology before the infection took place.

A discussion of the difficulties encountered in the diagnosis of lung cysts is related to the complications present. The true diagnosis is often made only at the time of exploratory thoracotomy. Thus, we have noted only nine instances that showed recognizable signs by x-ray film. The following abnormalities masked the underlying cystic disease in the remainder: Spontaneous pneumothorax referred to previously can readily mask underlying bulla, bleb or cyst formation. Again, when a bronchial block mechanism develops and in turn favors the retention of secreted mucus normally present within the cyst, x-ray changes will occur within the air cyst and it now resembles a tumor or, if situated in the hilum or mediastinum, a lymph node. Or, if situated in relation to the diaphragm, a cyst can be confused with a diaphragmatic hernia. If it is a "giant cyst" and contains fluid it is easily confused with an empyema. Finally, when a pyogenic infection attacks a lung cyst, the following could be diagnosed erroneously; lung abscess, bronchiectasis, tuberculosis, and acute pneumonitis. In this connection the axiomatic statements made by Adams[17] are illuminating: "A large pulmonary cavity presenting a fluid level unaccompanied by symptoms of sepsis or positive sputum for tubercle bacilli is most likely to be a lung cyst." He further stresses that in patients presenting evidence of chronic pneumonitis surrounding cystic areas,

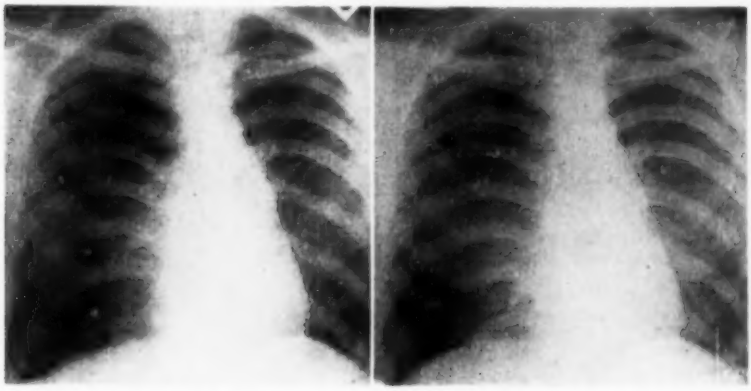

FIGURE 8 FIGURE 9

Figure 8: Spontaneous pneumothorax. Arrows point to edge of collapsed lung. Note pleural fluid.—*Figure 9:* Same case. Lung expanding. Arrows point to "blister" projecting from upper portion of collapsed lung, likely site of rupture.

the diagnosis of lung abscess is a common error. He lastly states that, "a history of insidious onset of a pulmonary suppurative process in a child without the usual etiologic factor for the production of lung abscess or bronchiectasis should strongly suggest the possibility of congenital cystic disease." This can be visualized in the adult as well.

The operative findings in cystic disease are informative. Cysts are found in any part of the chest cavity. Some are intimately associated with the lung parenchyma, and when opened are seen to have bronchial communications. These bronchial openings are situated at the base of the cyst. Some have a thin wall, while others, because of previous infection, can develop considerable wall thickness. Cysts are often attached to the cupola of the lung or to the pleura on its parietal or diaphragmatic surfaces. In most instances the pleural surfaces are non-adherent unless previous episodes of spontaneous pneumothorax have induced pleural irritation with resulting adhesions and/or symphysis. A small number of cysts are situated within the mediastinum. Preoperatively they are readily confused with lymphoma, teratoma, neuroma and pericardial coelomic cyst, etc.

SUMMARY

1. Respiratory embarrassment resulting from spontaneous pneumothorax is a frequent occurrence in this disease. The patient may have numerous cysts, even bilaterally, yet he will present litt.e if any respiratory distress unless a large cyst compresses normally functioning lung, in which case dyspnea is an outstanding symptom.

2. Roentgenological abnormalities encountered in cystic disease can readily obscure the underlying cystic pathology which was noted in over one-half of the cases described in this paper.

3. Spontaneous pneumothorax is a common manifestation of cystic disease. It can recur numerous times.

4. Diffuse unilateral or bilateral emphysema as an accompaniment of localized cystic disease was not found in this series of cases.

5. Although generally not thought of or known, infection and hemorrhage occur in cystic disease, and the basic pathology can readily be missed.

6. Exploratory thoracotomy is proving to be a realistic and fruitful approach to the problem of spontaneous pneumothorax, as well as the arrest of continuous dyspnea that is associated with cyst formation which is accompanied by compression of normal lung parenchyma.

Acknowledgement: I am indebted to the surgical and pathology staffs of the institutions listed below for the privilege of utilizing their records in the group of cases here discussed: Naval Hospital, Chelsea, Mass., Overholt Thoracic Clinic, Boston, Mass., Massachusetts Memorial Hospital, Boston, Mass., The John Adams Hospital of the Chelsea Soldiers Home, Sanatorium Division of the Boston City Hospital, Veterans Administration Hospital, Rutland Heights, Mass., Veterans Administration Hospital, West Roxbury, Mass., and Veterans Administration Hospital, Boston, Mass.

The illustrations were kindly reproduced from original x-ray films by Mr. Schaffer, Chief of the Photographic Laboratory of the Veterans Administration Hospital, Boston, Mass.

RESUMEN

1. El trantorno respiratorio producido por el neumotórax espontáneo es frecuente en esta enfermedad. El enfermo puede tener numerosos quistes aún bilaterales, y sin embargo puede haber poco trastorno respiratorio a menos que un gran quiste comprima el pulmón en su área normal en cuyo caso es la disnea el síntoma destacado.

2. Las anormalidades roentgenológicas encontradas en la enfermedad quística pueden facilmente obscurecer la patología quística subyacente como fué notado en más de la mitad de los casos descritos en este trabajo.

3. El neumotórax espontáneo es una manifestación común de la enfermedad quística. Puede recurrir numerosas veces.

4. El enfisema unilateral difuso o bilateral como acompañante de la enfermedad quística lozalizada no se encontró en esta serie.

5. Aunque generalmente no se piensa en ellas, la infección y la hemorragia ocurren en la enfermedad quística y la patología básica puede facilmente escaparse.

La toracotomía exploradora está demonstrando ser una táctica realista y fructuosa en el neumotórax espontáneo así como para detener la disnea continua asociada a la formación de quistes con compresión del parénquima normal.

RESUME

1. Le pneumothorax spontané est une affection dans laquelle la gêne respiratoire est fréquente. Le malade peut avoir de nombreux kystes, même bilatéraux, sans qu'il présente la moindre gêne respiratoire. Cependant, si un kyste volumineux compresse le poumon et fait obstacle à son fonctionnement normal, la dyspnée devient un symptôme majeur.

2. Des anomalies radiologiques qui s'associent à la maladie kystique peuvent complètement masquer les formations aériques sous-jacentes, Il en fut ainsi dans plus de la moitié des cas décrits dans cet article.

3. Le pneumothorax spontané est une manifestation banale de la maladie kystique. Il peut récidiver de nombreuses fois.

4. Dans cette série, la maladie kystique localisée ne s'accompagnait pas d'emphysème diffus, unilatéral ou bilatéral.

5. Une infection ou une hémorragie peut survenir au cours d'une maladie kystique que l'on ignore, ou à laquelle on ne rapporte pas ces complications, et la lésion primitive et causale peut passer parfaitement inaperçue.

6. La thoracotomie exploratrice se montre être une tentative réaliste et rentable dans le cas de pneumothorax spontané, aussi bien que pour faire cesser la dyspnée permanente due à la compression du parenchyme pulmonaire normal par une formation kystique.

ZUSAMMENFASSUNG

1. Behinderung der Atmung als Folge des Spontanpneumothorax ist ein häufiges Vorkommnis bei dieser Krankheit. Der Kranke kann viele Cysten haben, sogar auf beiden Seiten, und doch wird er wenig, wenn überhaupt, irgendwelche Störungen bei der Atmung bieten, solange nicht eine grosse Cyste eine normal arbeitende Lunge komprimiert, in welchem Fall die Dyspnoe ein hervorstechendes Symptom darstellt.

2. Röntgenologische Veränderungen, wie sie bei cystischen Krankheiten vorkommen, können die zugrunde liegende cystische Abnormalität verdecken, die in mehr als der Hälfte der in der vorliegenden Arbeit beschriebenen Fälle beobachtet wurden.

3. Der Spontanpneumothorax ist eine häufige Manifestation der Cystenkrankheit. Er kann sich viele Male wiederholen.

4. Ein duruses einseitiges oder beidseitiges Emphysem ist eine Begleiterscheinunge der lokalisierten Cystenkrankheit, die in der vorliegenden Reihe von Fällen nicht beobachtet wurde.

5. Obwohl man im allgemeinen nicht daran denkt oder es weiss, kann bei der Cystenkrankheit eine Infektion und eine Blutung auftreten, und die grundlegenden pathologischen Veränderungen können greifbar fehlen.

6. Die diagnostische Thorakotomie erweist sich als ein tatsächlicher und fruchtbarer Zugang zum Problem des Spontanpneumothorax, ebenso wie zur Hemmung einer anhaltenden Dyspnoe, die verknüpft ist mit der Cystenbildung und einer dadurch bedingten Kompression des normalen Lungenparenchyms.

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Minimal Active Tuberculosis: an Increasingly Difficult Diagnosis

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The diagnosis of minimal active tuberculosis is becoming annually more difficult because, paradoxically enough, of medical advances. A hundred years ago a physician was faced with a tuberculous patient "in a decline," and 30 or 40 years ago with a patient whose symptoms and physical signs suggested the need for a confirmatory roentgenogram of the chest. The situation began to change in 1931 when the Queensboro Tuberculosis and Health Association started to study the chests of well people radiographically on a small scale in the Borough of Queens, New York City, but it was not until early in World War II that the full impact of mass radiography became noticeable as a result of d'Abreu's development of practical photofluorography.[1] Chest lesions came then to be discovered in advance of symptoms or physical signs, and patients were brought to physicians in increasing numbers who were subjectively hale and hearty and had nothing wrong with them but suspicious shadows in roentgenograms of their chests.

No sooner did it appear that the early recognition of minimal tuberculosis had been simplified by this technological advance than the situation was complicated by recognition of the fact that the fungus diseases of the lungs, notably histoplasmosis and coccidioidomycosis, are common and that both, especially histoplasmosis, can produce radiographic changes hitherto thought to be produced exclusively by Mycobacterium tuberculosis.[2-5]

Most recently growing knowledge of and interest in the "atypical mycobacteria" has reached the point at which not even a report of a "positive sputum smear" (if the patient produces any sputum to stain) can be accepted as conclusive evidence that the patient has tuberculosis unless the organism can be grown in culture and identified as Mycobacterium tuberculosis.

The diagnostic problem is particularly acute in a military hospital because of the relative frequency with which members of the Armed Forces are examined photofluorographically and because its population is drawn from all parts of the United States including areas in which coccidioidomycosis and histoplasmosis are endemic.

To ascertain the extent of the problem we have reviewed the cases of the 166 members of the U.S. Navy and Marine Corps in which the diagnosis of minimal active tuberculosis was established on the Tuberculosis Service of the U.S. Naval Hospital, St. Albans, N.Y., in the three year period between October 1, 1953, and September 30, 1956. This number of cases is placed in perspective by noting that during the same period,

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among Navy and Marine Corps personnel, the diagnosis of moderately advanced tuberculosis was established in 227 cases and of far advanced in 100, while histoplasmosis was diagnosed in 28 instances and coccidioidomycosis in four. The results of the study are reported herewith.

Background Data

The 166 patients, including 2 women, ranged in age from 17 to 44 years. About two-thirds were less than 25 years old (Table I, a and b).

Of the patients, 156 (93.9 per cent) were Caucasoids, one (0.7 per cent) was a Malayan, and nine (5.4 per cent) were Negroids. This percentage of Negroids is somewhat less than the usual representation of that race on the Tuberculosis Service (about 11 per cent) and suggests that cavitation tends to occur earlier in the Negro.

Reasons for Admission

Only 29 (17.5 per cent) of these patients came to medical attention because of symptoms referable to, or possibly referable to, tuberculosis, while 128 (72.1 per cent) were found by routine radiography alone. The remaining nine patients (5.4 per cent) were hospitalized originally because of unrelated ailments (hernia, trauma, anxiety state, etc.) and their pulmonary lesions were detected by coincidental chest roentgenographic examinations (Table II).

Since mass radiography was little used 20 years ago and routine roentgenographic studies of the chest among general hospital admissions was seldom practiced, it is fair to conclude that at least four-fifths of these patients would not have come to the attention of a physician at that time. It is also fair to assume that, while many would have progressed to clinically obvious tuberculosis, many would have "cured" themselves spontaneously.

TABLE I—BACKGROUND DATA

a. Age:

Age Group	No.	Per cent
17-19	15	9.0
20-24	92	54.7
25-29	35	21.7
30-39	21	12.8
Over 40	3	1.8
	166	100.0

b. Race:

Race	No.	Per cent
Caucasoid	156	93.9
Negroid	9	5.4
Malayan	1	0.7
	166	100.0

TABLE II—REASONS FOR CASE DETECTION

Reason	Number	Per cent
Symptoms	29	17.5
Routine Radiography Alone	128	77.1
Other Ailments	9	5.4
	166	100.0

Roentgenographic Characteristics

Since the roentgenograms in these cases were interpreted and reported upon by several different roentgenologists who did not use uniform terminology, an exact tabulation of the roentgenographic findings is impossible. A review of the reports and of many of the films, however, shows that the following items were present, alone or in combination, and their approximate order of frequency (Table III):

The lesions were generally located in the apical-posterior segment areas of the upper lobes, that is in the locations commonly associated with reinfection tuberculosis, and all of the lesions persisted long enough to indicate that they represented a chronic disease process. Tracheobronchial and hilar lymphadenopathy was reported in but one case, in which no previous tuberculin reaction data were available. In retrospect this case and the four with "coin lesions" would probably be reclassified as primary tuberculosis.

The small number of instances in which fibrosis and calcification were reported indicates the freshness of the disease process in most of the patients.

Symptoms and Physical Signs

The paucity of symptoms has been indicated. As might be expected the temperature and pulse rate were seldom elevated, and physical examination was generally non-contributory except when it brought associated disease processes to light.

Tuberculin Reactivity

All of the 166 patients reacted to tuberculin, and previous reactivity was known in 85 cases, necessarily individuals young enough to have entered the service subsequent to 1949 when the routine testing of Navy and Marine Corps recruits was begun. Sixty-nine of these (81.2 per cent) were "Mantoux-negative" at that time, while the other 16 (18.8 per cent) were "Mantoux-positive." Evidently most of the infections were of recent origin and had occurred in early adult life.

Bacteriologic Findings

At least three cultures of the sputum or fasting gastric content were made upon admission and one culture monthly thereafter in each case. Adding the results of these cultures to reports of positive bacteriologic findings which accompanied some patients on admission, yields the disappointly low total of 70 cases bacteriologically positive by ordinary methods.

TABLE III—ROENTGENOGRAPHIC FINDINGS

Item	Reported
Exudation	96 Times
Nodulation	30 "
Exudation plus nodulation	24 "
Fibrosis and/or calcification	28 "
"Coin lesions"	4 "

Two further cases were proved by bronchoscopic aspiration culture. Thus only 72 (43.4 per cent) of the cases were bacteriologically positive clinically. Doubling the number of cultures per case would probably have increased the percentage of positive findings, but it is doubtful that anything short of making one culture each day for 30 days in each case—a practical impossibility—would have doubled it. Nor can the laboratory be blamed for during the same period, with the same number of specimens per case, it reported a high percentage of positivity in instances of cavitary disease.

Mycobacterium tuberculosis was identified by culture in all but two cases with positive sputum smear. One of these had received chemotherapy for a month prior to arrival.

Unfortunately the surgeon and the pathologist cannot be of too much help in this matter (Table IV). Examination of excised tissue in 22 cases subjected to resectional surgery added only nine instances of bacteriologic proof and failed to add or to confirm the clinical diagnosis in seven instances. In brief, only 15 (68.2 per cent) of the 22 surgical specimens were bacteriologically positive.

Thus by all methods of examination employed, only 81 (48.8 per cent) of the 166 patients with minimal tuberculosis were shedding enough tubercle bacilli to be demonstrated by the methods employed.

Conversion of the Mantoux Reaction as a Diagnostic Test

Conversion of an individual's Mantoux-reaction may be accepted as evidence that he has become infected with Mycobacterium tuberculosis at some time subsequent to the time of the negative reaction. A search of the records of the 85 bacteriologically negative shows evidence of such conversion in 37. Adding these 37 to the 81 cases in which Mycobacterium tuberculosis was recovered gives a total of 118 cases (71.1 per cent of the whole), in which the diagnosis of minimal active tuberculosis was established upon the basis of direct evidence.

Unproved Cases

In the 48 cases (28.9 per cent) in which neither bacteriologic proof nor conversion of the Mantoux reaction could be demonstrated, the diagnosis of minimal active tuberculosis was made perforce on the basis of clinical judgment, after evaluation of such evidence as came to hand. Of primary importance in this connection were attempts to exclude the presence of histoplasmosis or coccidioidomycosis. Considering all patients, 164 were tested intradermally with histoplasmin and coccidioidin antigens, of whom 20 (12.2 per cent) reacted to histoplasmin and 8 (4.9 per cent) to coccidioidin. The figure of 4.9 per cent closely approximates that found among all the patients admitted to this service, but the figure 12.2 per cent is

TABLE IV—BACTERIOLOGIC FINDINGS IN RESECTED SPECIMENS

		Surgical Specimen Bacteriology	
	Clinical Bacteriology	Cases Positive	Cases Negative
Cases Positive:	7	6	1
Cases Negative:	15	9	6
	22	15	7

considerably less than the usual harvest of 20 per cent reactions to histoplasmin intradermally.

All of the 48 patients considered to have tuberculosis on the basis of clinical judgment alone were tested with both coccidioidin and histoplasmin. Thirty-nine reacted to neither antigen, one to both antigens, one to coccidioidin, and seven to histoplasmin. Four of the latter were checked by means of the complement-fixation test, of whom three were negative while the fourth reacted with a titer of 1:8. It happened that this last was one of the few symptomatic patients, admitted because of gross hemoptysis, in whose case treatment for tuberculosis appeared to be mandatory on the basis of probabilities.

It is unfortunate that complement-fixation tests were not performed in all of these cases.

Primary Tuberculosis

In a group of cases made up largely of known "Mantoux-converters," the question arises as to whether or not many of the patients should not have been classified as primary tuberculosis. Evidently the younger patients correspond in general to the student population observed and reported upon by Myers et al,[6] and the roentgenographic findings often did not differ materially from the "early infiltrates in adolescents and young adults" described in the National Tuberculosis Association's "Diagnostic Standards 1955."[7]

During the three year period the diagnosis of primary tuberculosis was established in three cases not included in this series. All were known Mantoux-converters, one had classical right hilar lymph adenopathy with exudation in the posterior-basal segment, right lower lobe, another was known to have become Mantoux positive within a period of five months, and the third was an individual with a "coin lesion." Obviously the dividing line between minimal reinfection tuberculosis and primary tuberculosis in young adults is not clear-cut, in our minds at least.

Comment

Enough has been said to show that, as a practical matter, case finding by means of roentgenographic examination of the chest has far outstripped the ability of the microbiologist to provide an explanation for the observed phenomena. In the circumstances the clinician is often unhappily forced to make momentous decisions about his patients on the basis of incomplete evidence.

SUMMARY

1. Accurate diagnosis of minimal active tuberculosis has been rendered increasingly difficult due to
a. The large number of small, asymptomatic lesions detected by mass roentgenographic surveys.
b. Clinical recognition of the mycotic diseases, notably histoplasmosis and coccidioidomycosis, and
c. Increased knowledge of the "atypical" mycobacteria.
2. A review of 166 cases of minimal active tuberculosis among Naval and Marine Corps personnel over a three year period shows that
a. Four-fifths were admitted because of radiographic findings alone,
b. Bacteriologic proof was obtained in only 81 (48.8 per cent),
c. Recent conversion of the Mantoux reaction was demonstrated in 37 additional cases and was considered diagnostic,
d. Examination of excised tissue in 22 cases produced bacteriologic evidence in only 15 (68.2 per cent), and

e. The differential diagnosis of histoplasmosis and coccidioidomycosis was of primary importance.

3. The question is raised as to how many of these cases were examples of primary tuberculosis in young adults.

RESUMEN

1. El diagnóstico exacto de la tuberculosis mínima se viene haciendo cada vez más difícil debido a:

a. El gran número de lesiones pequeñas asintomáticas que se descubren por la roentgenfotografía.

b. El reconocimiento clínico de las enfermedades micósicas como la histoplasmosis principalmente y la coccidioidomicosis, y

c. Mayor conocimiento de las micobacterias atípicas.

2. La revisión de 166 casos de tuberculosis mínima activa en el personal de Cuerpo de Marina y del Cuerpo Naval de los Estados Unidos, durante 3 años ha mostrado:

a. Cuatro quintos se sujetaron a examen por hallazgos radiográficos solamente.

b. Se obtuvo prueba bacteriológica sólo en 81 (48.8 por ciento).

c. Se demostró la conversión reciente del Mantoux en 37 casos adicionales y se consideró de valor diagnóstico.

d. El examen del tejido resecado en 22 casos produjo evidencia bacteriológica sólo en 15 casos (68.2 por ciento), y

e. El diagnóstico diferencial de histoplasmosis y coccidioidomicosis fué de primordial importancia.

3. Se presenta el problema de cuantos de estos casos fueron ejemplos de tuberculosis primaria en adultos jóvenes.

RESUME

1. Le diagnostic précis de tuberculose minimale active a été rendu extrêmement difficile par:

a. le grand nombre de petites lésions asymptomatiques découvertes par les examens radiographiques systématiques;

b. la connaissance clinique des affections mycosiques, particulièrement l'histoplasmose et la coccidioidomycose

c. l'accroissement de nos connaissances sur les myco-bactéries "atypiques."

2. Une revue de 166 cas de tuberculose minime active parmi le personnel de la Marine, portant sur trois ans, montre que:

a. quatre-cinquième des cas furent admis par seules constatations radiographiques;

b. la preuve bactériologique ne fut obtenue que chez 81 malades (48,8%)

c. un virage récent de la réaction de Mantoux fut démontré dans 37 cas supplémentaires, et fut pris en considération comme valeur de diagnostic;

d. l'examen des tissus d'exérèse de 22 malades ne donna une preuve bactériologique que dans 15 cas (68,2%)

e. le diagnostic differentiel d'histoplasmose et de coccidioidomycose fut de première importance.

3. Les auteurs se demandent dans combien de ces cas s'agissait-il d'une tuberculose primaire chez de jeunes adultes.

ZUSAMMENFASSUNG

1. Die genaue Diagnose einer aktiven minimalen Tuberkulose hat sich im zunehmenden Masse schwierig gestaltet, also Folge von:

a. Der grossen Zahl kleiner symptomenloser Herde, die bei der Röntgenreihenuntersuchung gefunden werden.

b. Der klinischen Erkennung von Pilzkrankheiten, besonders Histoplasmose und Coccidioidomycose.

c. Zunehmender Kenntnis der "atypischen" Mycobakterien.

2. Eine Durchsicht von 166 Fällen von aktiver minimaler Tuberkulose bei Angehörigen des Naval und Marine corps während einer Zeitspanne von 3 Jahren zeigt, dass

a. vierfünftel eingewiesen wurden ausschliesslich wegen röntgenologischer Befunde allein.

b. Eine bakteriologische Bestätigung nur in 81 Fällen (48,8%) erlangt wurde.

c. Eine kürzlich erfolgte Konversion der Mantoux-Reaktion in 37 weiteren Fällen nachgewiesen und als von diagnostischer-Bedeutung angesehen wurde.

d. Untersuchung von excidiertem Gewebe in 22 Fällen einen bakteriologischen Befund nur bei 15 (68,2%) ergab und

e. die Differential-Diagnose von Histoplasmose und Coccidioidomycose von primärer Wichtigkeit war.

3. Es wird die Frage gestellt, wieviele von diesen Fällen Beispiele primärer Tuberkulose bei jugendlichen Erwachsenen waren.

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Bronchopulmonary Geotrichosis: A Review with Report of Four Cases

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Geotrichosis is an acute, subacute, or chronic infection of the mouth, bronchi, lungs, or gastrointestinal tract produced by one or more species of *Geotrichum*. This organism has never been carefully studied, but is known to be present often in the body without symptoms. Therefore, infection may arise from endogenous foci. Apparently a saprophytic fungus, it may become pathogenic under certain conditions, and like a few saprophytic bacteria, produce symptoms. Superimposed infection with *Geotrichum* may aggravate pre-existing pulmonary diseases such as bronchiectasis and pulmonary tuberculosis. The frequent association of *Geotrichum* and Friedländer's bacillus has been noted in the literature.[3]

Geotrichosis is rare and usually mild, but severe debilitation may occur. Only a few well-documented cases are reported in the medical literature. In 1933, Magalhaes[7] reported much experience with pulmonary geotrichosis in Brazil and described the disease in detail. Schnoor[9] in 1939, in a study of 314 stool specimens of medical students and nurses, and patients without gastrointestinal symptoms found *Geotrichum* in 29 per cent by culture.

Two cases of geotrichosis resembling chronic pulmonary tuberculosis were discovered by Reeves[8] in 1941, among 79 patients with bronchomycosis in the South.

Five of eight members of the same family were found to be endemic of pulmonary geotrichosis of an unknown species by Thjotti and Urdal[11] in 1949. Two of these exhibited x-ray chest films similar to pulmonary tuberculosis.

The clinical and x-ray film appearance of bronchopulmonary geotrichosis in two children, ages four and six, with cure using iodides and x-ray irradiation was described by Kunstadler and his associates.[5, 6] In a survey by Kunstadler and Milzer[6] in 1951 of the incidence of systemic mycotic infections in 211 children with acute respiratory disease, only one was positive to *Geotrichum* filtrate and one to *Geotrichum* filtrate and coccidioidin.

Geotrichum septicemia is noted in the literature. Bendove and Ashe[1] in 1952 isolated *Geotrichum* from the blood stream of a 79 year old diabetic. In the same year Kaliski and Beene[4] reported a *Geotrichum* septicemia without a primary site of origin complicating miliary tuberculosis in a two months old Latin-American male.

Symptomatology and Diagnosis

The mere finding of *Geotrichum* in the sputum does not warrant the diagnosis of geotrichosis for it may be playing a benign saprophytic role. The diagnosis of geotrichosis should be considered when the fungi are isolated in large numbers in repeated microscopic examinations of cultures from fresh specimens, bronchoscopic aspirates or biopsy, and after the

elimination of other diseases upon which it may be superimposed. *Geotrichum* intradermal tests prepared from the vaccine are useful in the diagnosis. A positive test may indicate past or present infection.

The frequently occurring oral white exudate of "Thrush" due to *Candida albicans* can not be differentiated microscopically from that due to *Geotrichum candidum*. *G. candidum* is often found in the stools of healthy people, but may lead to diarrhea with pus, mucus, and occasional blood in the stool. Large numbers of *Geotrichum* spores found in the stools decrease as symptoms subside.

People having symptoms of chronic bronchitis or pulmonary tuberculosis who expectorate a peculiar light-colored mucoid, gelatinous sputum bearing grayish flakes may have bronchopulmonary geotrichosis. The bronchial form is more frequent and presents the main symptom of persistent cough, as found in chronic bacterial bronchitis. In this form the general health is good and the temperature, pulse and respiration are rarely elevated. On physical examination many coarse rales may be heard in the pulmonary bases.

Pulmonary geotrichosis usually presents fever, rapid pulse and respirations and leukocytosis. Blood-tinged sputum may or may not be present, and frank hemoptysis occurs seldom. There may be dullness to percussion, altered breath sounds, and fine and medium rales over the involved area. Organisms are abundant in the flakes occurring in the sputum. This type, incidentally, often resembles acute reinfection tuberculosis.

Roentgenograms of the chest are not specific. Bronchial geotrichosis usually presents a non-specific diffuse peribronchial infiltration which may extend as fine strands into the periphery, or into the bases. The pulmonary form shows homogenous dense areas of infiltration which may occur in any lobe, but more often in the upper. Thin-walled cavities may, or may not, be present. The x-ray film may be indistinguishable from pulmonary tuberculosis. Serial roentgenograms are important in diagnosis.

In the differential diagnosis, bronchomycoses, in particular, candidiasis, cryptococcosis, coccidioidomycosis, histoplasmosis, nocardiosis and North American blastomycosis must be considered. Chronic bronchitis, atypical pneumonia, bacterial pneumonia, pulmonary fibrosis and pulmonary brucellosis may simulate the disease.[10]

Mycology

Geotrichum was first isolated and described from the leaf mold by Link in 1809. Brumpt,[7] in 1936, listed 20 species reported by different authors.

Geotrichum candidum is a yeast-like fungus which reproduces by segmentation of hyphae into oblong or rectangular (at times, somewhat spherical) arthrospores with rounded ends and with a characteristic germ tube arising from one corner. The arthrospores measure 4 to 8 microns in length by 4 to 10 microns in diameter. Confusion may exist with the filamentous *Coccidioides immitis* which produces arthrospores, the filamentous sputum contaminant *Oospora*, and the budding forms of Blastomyces. Direct examination of a thin film of fresh material cleared with 10 per cent potassium hydroxide placed under a cover slip is often satisfactory. The arthrospores may appear dark with Gram's stain.[3]

Sputa or feces may be streaked on Sabouraud's glucose agar on which *G. candidum* grows at room temperature within two weeks. Antibiotics are desirable to prevent masking by bacterial contaminants. The colonies are characteristically white or cream-colored, flat, mealy, membranous and yeastlike in appearance and are easily lifted by a wire loop. A white pellicle appears in honey broth or other liquid media.

Pathogenicity for laboratory animals has not been demonstrated.

Prognosis and Treatment

The prognosis of geotrichosis is usually excellent and the disease may terminate without treatment. *Geotrichum* stomatitis may be resistant to treatment at times but usually responds to local application of 2 per cent gentian violet solution twice daily for seven days, or sodium perborate mouth wash. Prescription of vitamin B-complex is desirable. The intestinal type has responded well to gentian violet enteric-coated tablets 0.06 gram with each meal three times daily for 30 days.

In the bronchial and pulmonary infections, bed rest is advisable, overexertion and fatigue should be avoided, and a high caloric, high vitamin diet is recommended. A saturated solution of potassium iodide is recommended with dosage of five drops in water three times daily, increased by one drop daily until signs of intolerance occur. The dosage should be maintained below this level for weeks or months until cure is perfected. Intravenous gentian violet may be used, giving 5 mgms. per kgm. of weight diluted to 5 per cent daily for seven doses.

Where failure of the above medications occurs, the *Geotrichum* autogenous vaccine may be used according to the method of Conant in the treatment of blastomycosis.

Clinical Material

Case 1: Pulmonary tuberculosis appearing three years after the diagnosis of *Geotrichum* bronchitis and continuing simultaneously.

Case 2: Pneumonia of the right upper lobe with the dual culture of Friedländer's bacillus and *Geotrichum candidum*.

Case 3: Bronchial geotrichosis superimposed upon pulmonary emphysema.

Case 4: Pulmonary geotrichosis of the left upper lobe with patchy infiltration and cavitation and an associated *Geotrichum candidum* septicemia.

Case 1. L.A.W. Feb. 3, 1945, is a 22 year old married, white housewife, mother of four children, who had experienced the onset of weakness, cough productive of yellow mucoid sputum with small gray specks interspersed for the past four months. She was said to have had bronchitis followed by pneumonia. There had been no hemoptysis.

Temperature was 99.4° F., pulse 82, respirations 20. Weight was 104 pounds. The mouth and throat revealed a white exudate suggestive of thrush. Examination of the chest revealed normal resonance, but many coarse rhonchi in both bases. An x-ray film of the chest revealed moderate increase in peri-bronchial markings. Repeated smears and cultures of the oral exudate and the sputum revealed *Geotrichum candidum*. Twelve Ziehl-Neelsen stains, three cultures and a guinea pig inoculation were negative for *Mycobacterium tuberculosis*. Tuberculin 1:1000, histoplasmin, coccidioidin tests were negative. Hemoglobin was 12.0 grams, erythrocyte count 3,680,000, leukocyte count 11,250 with 75 per cent polymorphonuclear leukocytes, sedimentation rate 16 mm., and blood culture negative. Stool examination was positive for *G. candidum* by culture. She was treated with potassium iodide by the rapid method with symptomatic improvement.

There was an exacerbation of the bronchitis April 1947. Cultures remained unchanged. A bronchoscopic examination revealed a white exudate in the bronchi bilaterally. Culture of scrapings of this exudate revealed *G. candidum* but was negative for *M. tuberculosis*.

She was seen next on March 24, 1948, with hemoptysis, temperature 101° F., pulse 96 and respirations 22. Roentgenologic study of the chest revealed a small calcified nodule in the parenchyma of the right lower lobe and heavy soft infiltration in the circle of the first rib and first two interspaces. There was a large cavity in the first interspace. The left lung showed scattered soft infiltration in the second, third and fourth interspaces (Figure 1). At this time, Ziehl-Neelsen stain revealed numerous acid-fast organisms (Gaffky 5) and cultures were positive for *M. tuberculosis* and *Geotrichum candidum*. She was placed on bed rest, pneumoperitoneum and streptomycin, and later, paraaminosalicylic acid.

May 9, 1950, an x-ray film of the chest showed mottling throughout the right lung with a cavity at the level of the clavicle, above and below, and multiple small cavities in the left lung. Cultures for both *M. tuberculosis* and *G. candidum* remained positive.

By June 25, 1954, the tuberculosis had become arrested. Sputa were negative for acid-fast organisms, but the culture for *G. candidum* remained positive. Chest x-ray films September 29, 1955, and March 6, 1956, revealed no sign of activity. On the latter date, culture for *G. candidum* was found negative for the first time. The case will be followed.

Comment: This case was followed for a period of three years with oral and bronchial geotrichosis, proved by scrapings from the exudate in the mouth and bronchoscopically. This was followed by active pulmonary tuberculosis, accompanied by positive cultures for *G. candidum*. After six years, the pulmonary tuberculosis became arrested, but there was cultural evidence of *G. candidum* for another two years.

Case 2. J. B. December 28, 1954, this 64 year old white, married, retired railroad engineer who had had Parkinson's disease for about five years, complained of a racking cough productive of grayish mucoid sputum, dyspnea and fever of three weeks duration. Past history was irrelevant.

Temperature was 101.8° F., pulse 88, respirations 24. He appeared somewhat cyanotic and dyspneic. There was slight dullness to percussion, suppressed breath sounds and many sibilant rales over the right upper chest. The leukocyte count was 13,400 with 76 per cent polymorphonuclear leukocytes. Sputum culture was positive for Friedlander's bacillus and culture on Sabouraud's medium grew *Geotrichum candidum*. X-ray film of the chest showed moderate, generalized cardiac hypertrophy, and consolidation of the right upper lobe, suggestive of lobar pneumonia (Figure 2).

There was a prolonged febrile course in which little change clinically or roentgenologically was noted. Both the Friedlander bacillus and Geotrichum remained in the

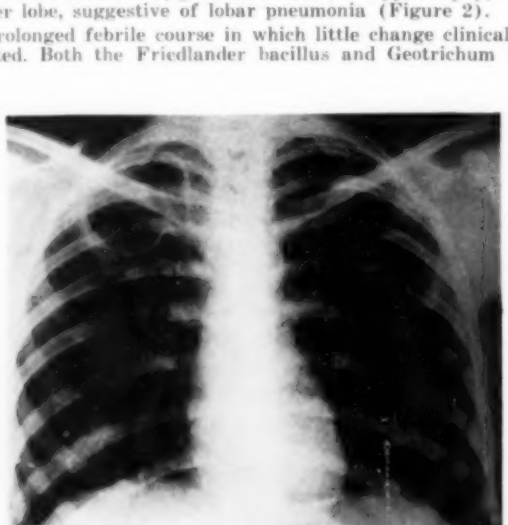

FIGURE 1: Case 1, L. A. W., x-ray film of chest, March 24, 1948, showing heavy soft infiltration and large cavity of right upper lobe, and scattered infiltration in left lung.

sputum. Bronchoscopy March 15, 1955, revealed no neoplasm, but study of the exudate from the right upper lobe disclosed myriads of both organisms. Three cultures for *Mycobacterium tuberculosis* were negative. The PPD (Double strength), histoplasmin, and coccidioidin tests were negative. Guinea pig inoculation was negative.

Treatment with bed rest, supportive measures, aureomycin, sulfadiazine, streptomycin and iodide was continued. By September 15, 1955, an x-ray film of the chest was clear. Cultures were no longer positive for either the bacteria or fungi.

Discussion: This case illustrates the simultaneous occurrence of Friedländer's bacillus and *Geotrichum candidum* in the production of pneumonia. Such a dual infection has been recorded previously. This combination leads to prolonged resistant pneumonia in which both organisms play a marked role.

Case 3. C. J. R. October 24, 1955. This is a 66 year old white, retired merchant who has had chronic cough productive of jelly-like grayish, gritty mucoid sputum for the past 15 years. He has felt dyspneic, but apparently runs no fever. He smokes a pipe infrequently.

Physical examination discloses temperature 98.4° F., pulse 82, respiration 20. He is well developed but poorly nourished. Thorax is barrel-shaped. Chest is hyperresonant, breath sounds are distant and there are many sibilant rales throughout both lungs. The heart is enlarged to the left, but rhythm is normal and there are no murmurs. The peripheral vessels are sclerotic and tortuous. The blood pressure was 124/60.

Roentgenogram of the chest revealed marked infiltration throughout the entire chest and early emphysema. PPD (Double strength) and histoplasmin tests were negative. Ten Ziehl-Neelsen sputum smears were negative for acid-fast bacilli. Sputum culture for *M. tuberculosis* was negative, but on Sabouraud's medium grew *Geotrichum candidum* in serial cultures. The *Geotrichum* skin test was strongly positive. Guinea pig inoculation was negative. Hemoglobin was 14.0 grams, erythrocyte count 4,300,000, leukocyte count 6,050.

It was felt he had a *Geotrichum* bronchitis. Treatment with potassium iodide led to improvement. X-ray film of the chest March 9, 1956, showed fewer markings in the lungs. Culture for *G. candidum* remained positive. Treatment will be pursued.

Comment: Bronchial geotrichosis is considered to be the more common of the broncho-pulmonary infections due to *G. candidum*. This case represents an emphysema complicated by geotrichosis.

Case 4. R. W., January 5, 1952. For two months this 52 year old farmer had noticed progressive cough productive of thick, grayish, gelatinous sputum. There had been afternoon fever, night sweats and weakness. He had lost 10 pounds of weight. An x-ray film of the chest one year previous was negative. Two weeks ago there was hemoptysis and the sputum smelled foul. There was no chest pain but slight exertional dyspnea.

Physical examination showed a well developed, well nourished man with slight dyspnea, temperature 100.4° F., pulse 100 and respirations 24. There was dullness

FIGURE 2: Case 2, J. B., x-ray film of chest, December 28, 1954, displaying consolidation of right upper lobe suggesting lobar pneumonia.

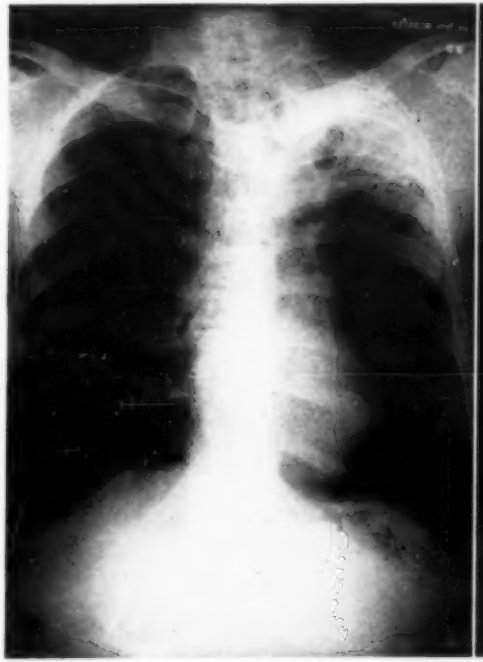

FIGURE 3

FIGURE 4

FIGURE 5

Figure 3: Case 4, R. W., January 5, 1952, x-ray film of chest showing patchy infiltration and cavitation of left upper lobe.—*Figure 4:* Case 4, Culture of *G. candidum* on Sabouraud's glucose agar.—*Figure 5:* Case 4, Smear from culture in Figure 4, showing arthrospores of *Geotrichum candidum*.

to percussion over the left upper lobe anteriorly, bronchial breath sounds, and many sibilant and fine moist rales over the same area. Remainder of examination was negative.

Roentgenograms of the chest revealed a smooth, patchy infiltration and cavitation in the left upper lobe (Figure 3). PPD (Double strength), histoplasmin, and coccidioidin tests were repeatedly negative. Twenty-four sputa were negative for acid-fast bacilli, as well as gastric washings. Five sputa cultures for *M. tuberculosis* have been negative. Guinea pig inoculation for tuberculosis was negative. Eight cultures for *Geotrichum candidum* have been positive (Figures 4, 5). Bronchoscopic examination revealed no evidence of neoplasm but culture was positive for *G. candidum*, negative for *M. tuberculosis*. Geotrichum cutaneous tests been consistently positive. On one occasion, following a chill, a blood culture was positive for *G. candidum*.

The routine blood counts have shown a mild hypochromic microcytic anemia. Leukocyte counts have ranged from 7,800 to 12,000. Fasting blood sugar, non-protein-nitrogen, liver function series, Kline test and urinalysis have been normal.

Prolonged treatment with oral potassium iodide and intravenous gentian violet have resulted in disappearance of symptoms. By July 1, 1955, the chest x-ray film was normal, leaving no residual changes. He will continue to be followed closely. Cultures for *G. candidum* remained positive for 30 months.

Comment: This patient demonstrated a primary, patchy infiltration with cavitation of the left upper lobe. Treatment with oral iodides and intravenous gentian violet has been successful.

Discussion: Since more reliance is being placed upon the etiologic agent and less upon the specific x-ray film diagnosis of pulmonary diseases, the importance of bronchopulmonary mycoses has increased. Many fungi which are considered saprophytic may become pathogenic to man and become disseminated under conditions favorable to their growth. Such a fungus is *Geotrichum* which grows in soil and decaying vegetation, but which may thrive in the gastrointestinal and upper respiratory tract of healthy people. From such endogenous foci, the organism may become pathogenic as a primary or secondary invader.

The isolation of *Geotrichum candidum* from the sputum does not necessarily establish it as a clinically significant virulent agent. Its isolation should stimulate further search in the differential diagnosis. Repeated abundant growth in sputa, bronchial aspirates, biopsies and the exclusion of other respiratory diseases capable of presenting the same clinical picture should precede the diagnosis of bronchopulmonary geotrichosis. It should be remembered that no typical clinical or roentgenologic picture typifies the disease.

Case 1 was treated for three years for *Geotrichum* bronchitis, following careful exclusion of pulmonary tuberculosis by negative cultures, guinea pig inoculation, tuberculin and bronchoscopic studies. Nevertheless, this was followed by active pulmonary tuberculosis which became arrested after six years, but positive cultures for *G. candidum* persisted for two years longer.

The exclusion of pulmonary tuberculosis is important before treatment with iodides in every instance. The secondary invasion, or superimposition upon bronchiectasis, pulmonary tuberculosis and other chronic pulmonary diseases may be a common occurrence.

Case 4 represents one of cavitation and infiltration of the left upper lobe due to *G. candidum*. This was confirmed by repeated cultures, sputa studies, cutaneous tests and by bronchoscopic aspirate. A *Geotrichum* septicemia was present. This has been preceded by only two such reports

in the literature and a third being reported separately by the author. Cure by the use of iodides occurred.

SUMMARY

Four cases of bronchopulmonary geotrichosis, proved by repeated cultures of sputa, bronchial aspirates and *Geotrichum* cutaneous tests, are reported. One was of *Geotrichum* bronchitis of three years duration, followed by simultaneous appearance of pulmonary tuberculosis for six years. One case of *Geotrichum* bronchitis was superimposed upon pulmonary emphysema. The dual appearance of *Geotrichum candidum* and Friedlander's bacillus was found in pneumonia of the right upper lobe. Finally, a primary, patchy infiltration and cavitation due to *G. candidum* in the left upper lobe and an accompanying septicemia was diagnosed in case 4.

Treatment with iodides was successful in the cases of *Geotrichum* bronchitis and has produced gradual roentgenographic and clinical improvement in the case of pulmonary geotrichosis with cavitation and septicemia.

RESUMEN

Se relatan cuatro casos de geotricosis pulmonar comprobados por repetidos cultivos de esputos, productos de aspiración bronquial y pruebas cutáneas de geotricum.

En uno, se trataba de bronquitis con tres años de duración seguida de apariencia de tuberculosis pulmonar por seis años. Un caso de bronquitis de geotricum se implantó sobre enfisema pulmonar.

La doble aparición de *geotricum candidum* y bacílo de Friedlander se observó en neumonía del lóbulo superior derecho. En el cuarto caso, por último, se vió una infiltración moteada con excavación debidas a *G. candidum* en el lóbulo superior izquierdo con septicemia acompañante.

El tratamiento con yoduros fué eficaz en los casos de bronquitis de geotricum y ha producido mejoría clínica y radiológica en el caso de geotricosis con excavación y septicemia.

RESUME

L'auteur rapporte quatre cas de géotrichose bronchopulmonaire mise en évidence par des cultures répétées sur expectoration, des aspirations bronchiques, et des tests cutanés au Geotrichum. L'un fut un cas de bronchite à geotrichum, d'une durée de trois ans, suivie par l'apparition simultanée d'une tuberculose pulmonaire qui dura six ans. Un cas de bronchite à géotrichum se superposa à un emphysème pulmonaire. La double apparition de *candidum geotrichum* et de bacilles de Friedlander fut constatée dans une pneumonie du lobe supérieur droit. Enfin, pour le quatrième cas on diagnostiqua une infiltration primaire nodulaire et excavée due au *G. candidum* dans le lobe supérieur gauche, et s'accompagnant de septicémie.

Le traitement par les iodures fut satisfaisant dans les cas de bronchite à geotrichum et produisit une amélioration clinique et radiologique progressive dans le cas de geotrichose pulmonaire accompagnée de caverne et de septicémie.

ZUSAMMENFASSUNG

Bericht über 4 Fälle von bronchopulmonaler Geotrichose, die bestätigt wurden durch wiederholte Kulturen vom Sputum und Bronchialsekret und Hautproben auf Geotrichum. Einmal handelte es sich um eine geotrichale Bronchitis von 3-jähriger Dauer, an die sich eine gleichzeitige Lungentuberkulose von 6-jähriger Dauer anschloss. Ein Fall von geotrichaler Bronchitis war überlagert durch ein Lungenemphysem. Das 2-fache Auftreten von *Geotrichum candidum* und Friedländer's Bazillus fand sich bei einer rechtsseitigen Oberlappenpneumonie. Schliesslich wurde eine primäre fleckige Infiltration und Cavernisierung durch *G. candidum* im linken Oberlappen und eine begleitende Septicaemie im Fall 4 diagnostiziert.

In den Fällen von geotrichaler Bronchitis war eine Jodbehandlung von Erfolg begleitet und bewirkte schrittweise röntgenologische und klinische Besserung im Fall der pulmonalen Geotrichose mit Cavernisierung und Septicaemie.

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Intralobar Pulmonary Sequestration Associated with Anomalous Pulmonary Vessels: a Nonentity

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Many instances of severe localized lung damage characterized by a systemic blood supply are recorded in medical literature. The usual designation is pulmonary sequestration related to an anomalous or aberrant artery, with the inference that the basic change is a congenital malformation.

The surgical hazard created by large aortic branches in unexpected situations justifies these reports. However, many of them are presented on the theoretical basis of a congenital etiology, and some have amplified and tabulated the clinical features for the purpose of providing preoperative clinical diagnoses. While a congenital etiology cannot be denied absolutely, it is unproved, and we consider it illogical to clinically diagnose pathologic states of uncertain existence.

Many English and foreign language publications were reviewed. Fewer cases were encountered in the latter group, otherwise, there was no significant difference in the character and type of reported cases. This disorder is occasionally reported under other classifications, such as congenital cysts, accessory lobes, and aberrant lung tissue. References one to 27 include most of the cases reported as sequestrations in modern English medical literature. We feel that the available evidence favors an etiology based on pathologic processes, and that practically all the cases reported as congenital anomalies are erroneously recorded.

Definition of Terms: We believe intrapulmonary sequestration is the result of bronchopulmonary disease and frequently confused with ordinary advanced, progressive or burned out, bronchiectatic and cystic inflammatory changes, and also find it occasionally confused with aberrant and accessory lung anomalies when they are accompanied by unusual vessels.

Aberrant anomalies[28, 29] are characterized by fetal lung, bronchial elements, mucinous cysts, aortic arterial supply and azygos venous return. They usually fail to exhibit pleural or bronchovascular connections with the lung but have stalks to the esophagus or other portions of the gastrointestinal tract, or to the diaphragm. Frequently they are accompanied by other anomalies, and have been distinguished from accessory types of lung anomalies.[30] These are usually recognizable as part of the existing lung with distinct bronchovascular connections. Azygos and tracheal accessory lobes are examples. Neither of these conditions harbors the typical morbid anatomy of intralobar sequestration, namely: thickening, dilatations, and mucinous cystic collections of the bronchi, atelectasis, fibrosis, and chronic cellular inflammatory infiltration of the parenchyma, and degenerative vascular changes. These are the changes of severe and advanced bronchopulmonary disease. They seem to acquire the title of sequestration only when accompanied by an unusual artery. There is some question whether

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the aberrant type should be regarded as sequestration at all, even if the modifying term, "extralobar" is added, for sequestration implies, at least, a former connection or continuity with the parent structure. As mentioned before, these anomalies do not indicate the existence of such a connection, in contrast to sequestrations and accessory forms, and probably represent foregut derivations.

Theories

Congenital: Most of the cases have been recorded since 1946 when Pryce[6] first proposed the sequestration theory which implies ischemic necrosis of a portion of the developing lung from pressure exerted by an anomalous vessel. He regarded the offending vessels as pulmonary rather than systemic because of their histologic composition. Smith[23, 24] initially accepted this theory, then discarded it, and proposed a developmental defect of a portion of the pulmonary artery as the basic etiology. Fry[20] offered a congenital sequestration of the primitive foregut near the caudal end of the laryngotracheal groove as an explanation.

Acquired: Pryce noted the close correlation of species in the cases he reported. Smith and many other authors except Fry mentioned sepsis as an etiologic possibility; however, Boyden[31] first placed "sequestration" in quotes, and considered a congenital etiology less acceptable than one based on a pathologic process.

Discussion

Fry's theory of foregut sequestration seems an acceptable theory for an aberrant anomaly without a pulmonary stalk, such as reported by Deaton,[32] but not for an area of sequestration in an anatomically intact lobe. While it must be acknowledged that defective development of the pulmonary artery, as suggested by Smith, might provide strong stimuli for the development of prominent systemic vessels, it fails to explain those cases exhibiting pulmonary arterial branches in the sequestered area. In addition, cases of absence and hypoplasia of the pulmonary artery, as reported by Maier,[33] are not singularly accompanied by the bronchopulmonary changes characteristic of sequestration, unless the element of sepsis is present or cannot be excluded. Furthermore, Ingalls[34] noted the constancy of the pulmonary circulation except in outspoken cases of cardiovascular anomaly.

Even with special stains histologists may find difficulty in classifying the arteries in markedly diseased lung tissue. Advanced hypertrophy of a small aortic branch may produce varied alterations in its muscle and elastic tissue composition. We feel that this composition may be considerably influenced by blood pressure and flow, and that it might be an unreliable criterion of vessel origin. Detailed histologic studies of the so-called anomalous vessels were not recorded in the majority of cases we reviewed.

Absence of pigment does not necessarily support a congenital etiology, for any process which persistently prohibits ventilation of a part of the lung, and starts early in life, will prevent pigmentation of that part. Some authors regard the absence of a communication between the bronchial tree and the involved area of lung necessary for the classification of sequestra-

tion; others do not, and report cases exhibiting such passages. In still others, communications were not demonstrated at operation or in the specimen, but preoperative x-ray films disclosed air in the cystic lung spaces. We know that failure of contrast media to fill a given bronchus does not mean that it is occluded, and that tight, edematous bronchostenoses have been regarded frequently as blind cul-de-sacs when viewed bronchoscopically. The functional and organic "shut off" of a portion of the bronchial tree in protracted, severe, destructive bronchial inflammations is not uncommon, and explains many of the cases of nonpigmentation and atelectasis, as well as the difficulties in the demonstration of bronchial passages at operation and on the specimen board.

Along the same lines we feel that pulmonary angiograms are frequently misinterpreted. If contrast medium fails to fill a pulmonary artery, it only means that an insuffient concentration was present at a given point the moment the film was exposed, not that the pulmonary artery is absent or obstructed. Thus one of Maier's cases is not a proved absence of the pulmonary artery. After failing to demonstrate dye in one pulmonary artery with excellent filling of the opposite side, at operation we have found intact, unobstructed pulmonary arteries filled with pink blood. This blood is relatively static, or even flowing in a reverse direction, its source being the numerous bronchopulmonary arterial anastomoses consequent to the pulmonary disease. Contrast media will not enter these vessels in sufficient concentration for radiologic demonstration despite their patency. Figure 1.

Clinical experiences[35] in the surgical treatment of destructive inflammatory pulmonary diseases repeatedly demonstrate the transfer of blood flow from the pulmonary to the systemic arteries, particularly the intercostal and bronchial aortic branches. This shift has been recognized for years,[36] repeatedly produced experimentally, and its demonstration, as well as its physiologic implications, recently emphasized by Liebow and

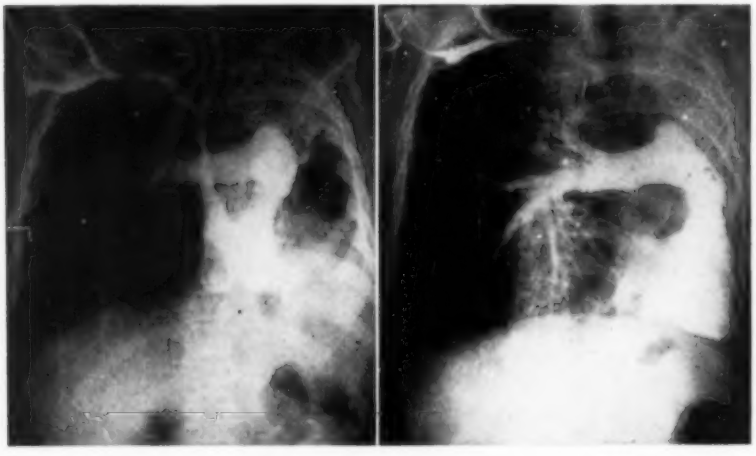

FIGURE 1: Two separate instances of pulmonary angiography with failure of sufficient contrast medium in left pulmonary artery to permits its visualization. Bronchopulmonary anastomosis in diseased left lung cause relative stasis or reverse flow in left pulmonary artery which is patent and unobstructed. See text.

other authors.[37-40] It seems to be easily invoked by pulmonary artery occlusion, especially early in life, and by destructive inflammations. We believe it responsible for the development of systemic collateral pulmonary vessels, which are too frequently regarded as congenital anomalies. Figure 2 concerns a 45-year-old woman regarded from childhood as an agenesis of the left lung, but actually an instance of septic destruction of an intact lung with normal vessels, secondary to cystic bronchiectasis resulting from pre-existing bronchostenosis. There is no reason to regard the huge systemic vessel a congenital anomaly; although it is unusual, it reasonably can still be called a hypertrophic bronchial artery.

We regard the arterial system of the mediastinum, central pleura, lung root and bronchi a complex network of small arteries with innumerable existing and potential communications. The bronchial, esophageal, pericardial, intercostal, internal mammary, superior and inferior phrenic arteries are some with names that contribute to this network. Other aortic branches in the inferior pulmonary ligament, mediastinum, and even those of the trunk and upper abdomen are potential components of this system. As found by Cauldwell[41] and others,[42] the bronchial arteries may vary widely in site of origin. In view of their striking response to certain lung conditions and their prominent role in this network, we consider them capable of producing tremendous developments and expansions of portions of this network thereby creating unusual or anomalous aortic vessels. The astounding proliferation of this system, produced in newborn puppies by pulmonary artery occlusion as reported by Liebow,[43] particularly emphasizes the possibility of similar processes occurring in man, especially if a severe pulmonary inflammation is attended by pulmonary artery thrombosis during infancy. Consequently, we feel that most "sequestrations" with so-called anomalous and aberrant vessels are areas of destructive bronchopulmonary disease with hypertrophic and newly developed vessels belonging to the network of the bronchial and mediastinal arteries.

Of 96 cases reviewed, 83 had a history of significant pulmonary infection or the surgical specimen exhibited open bronchiectasis, and it would be reasonable to regard the anomalous vessel a component of a local expansion of the bronchomediastinal arterial network. In 10 others the history was omitted or there was no history of pulmonary infection. Nine of these were mucinous bronchial cysts and could well represent "burned out" infections. We regarded only three cases as possibly true anomalies; all of these were associated with diaphragmatic hernias. The mean age of the cases was 21 years, the oldest 60, the youngest 20 months; only three were under three years. Many cases gave a history of pulmonary disease extending back many years, frequently to childhood and infancy. It is unusual for an adult to recall the details of his infancy unless he has been told about a "double pneumonia." No history of a pulmonary ailment does not exclude the possibility, and we consider it more reasonable to assume a preceding pulmonary disease in such circumstances, than to consider every case an instance of infection occurring in an area of congenital malformation.

Aberrant lung anomalies are more rare than the accessory type; both are unquestionably congenital and therefore occasionally encountered at autopsy of the newborn. On the other hand, thousands of such autop-

FIGURE 2A

FIGURE 2B

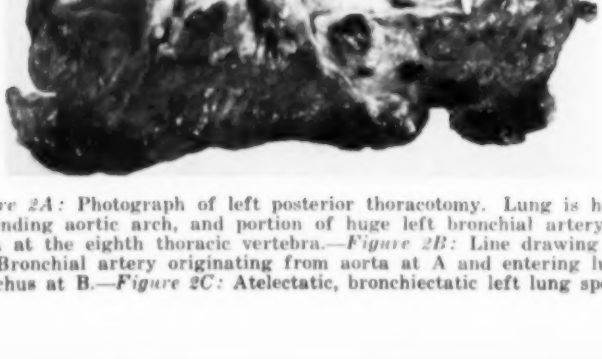

FIGURE 2C

Figure 2A: Photograph of left posterior thoracotomy. Lung is held down, showing descending aortic arch, and portion of huge left bronchial artery arising from the aorta at the eighth thoracic vertebra.—*Figure 2B:* Line drawing for orientation of A. Bronchial artery originating from aorta at A and entering lung with the main bronchus at B.—*Figure 2C:* Atelectatic, bronchiectatic left lung specimen.

sies[21, 44] have not disclosed any instance of typical intralobar sequestration with an anomalous pulmonary artery.

Consideration of this fact, along with the evidences from cases reviewed, and the arguments in the preceding discussion, indicates that it might be better to abandon the term intralobar pulmonary sequestration, than to continue its loose usage of the past.

SUMMARY

1. We consider intrapulmonary sequestration the result of pathologic processes rather than the effect of a congenitally anomalous pulmonary vessel. This applies to practically all the cases reported in the literature as congenital anomalies.

2. We find it confused with bronchiectasis, cystic disease, accessory and aberrant lung anomalies.

3. The arterial system of the mediastinum, particularly the bronchial arteries, is capable of astounding developments in response to severe, prolonged, bronchopulmonary infections, especially to those occurring early in life, and accompanied by some degree of pulmonary artery obstruction.

4. The absence of this condition in thousands of autopsies of the newborn is singularly striking.

RESUMEN

1. Consideramos la secuestración intrapulmonar el resultado de un proceso pathológico más bien que el resultado de un vaso pulmonar anómalo. Esto se aplica prácticamente a todos los casos relatados en la literatura como anomalías congénitas.

2. Encontramos una confusión entre bronquiectasia, enfermedad cística, y anomalías accessorias y aberrantes del pulmón.

3. El sistema arterial del mediastino, en especial las arterias bronquiales, es capaz de sorprendentes cambios en respuesta a infecciones graves broncopulmonares especialmente en las que ocurren al principio de la vida y que se acompañan de cierto grado de obstrucción arterial.

4. La ausencia de esta condición en millares de autopsias del reciennacido es singularmente notable.

RESUME

1. Les auteurs considèrent la séquestration intrapulmonaire comme le résultat de processus pathologiques plutôt que comme la conséquence d'une anomalie vasculaire. Cette conception se rapporte à tous les cas publiés dans la littérature comme anomalies congénitales.

2. Les auteurs constatent que cette affection est condonfue avec la bronchiectasie, la maladie kystique, et les anomalies pulmonaires secondaires et aberrantes.

3. Le système artériel du médiastin, particulièrement les artères bronchiques, est susceptible de développements surprenants à la suite des infections bronchopulmonaires graves et prolongées, particulièrement après celles qui surviennent précocément et qui sont accompagnées d'un certain degrée d'obstruction de l'artère pulmonaire.

4. L'absence de cette condition dans des milliers d'autopsies de nouveaux-nés est singulièrement frappante.

ZUSAMMENFASSUNG

1. Wir halten eine intrapulmonale Sequesterbildung eher für die Folge eines pathologischen Prozesses als die Auswirkung von angebornen abnormen pulmonalen Gefässen. Dies ist anwendbar auf praktisch alle in der Literatur als angeborene Anomalien angegebenen Fälle.

2. Wir finden dieses Geschehen verwechselt mit Bronkiektasie, Cystenkrankheit, abzessorischen und von der gewöhnlichen Form abweichenden Lungen-Anomalien.

3. Das arterielle Gefässsystem des Mediastinums, besonders der Bronchial-arterien ist erstaunlicher Entwicklung fähig als Reaktion auf schwere, anhaltende bronchopulmonale-Infektionen besonders bei solchen, die sich im frühkindlichen Leben abspielen und begleitet sind von einem bestimmten Grad einer Pulmonalarterienstenose.

4. Das Fehlen dieser Veränderung bei Tausenden von Autopsien von Neugeborenen ist besonders überzeugend.

Complete reference list and an addendum concerning additional cases and Boyden's new theory will appear in reprints.

Responsibility for Tuberculosis Case Finding: Changing the Approach

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Who is responsible for finding tuberculosis? Those to whom it matters. Thus far, the ones to whom it matters have been few: the public health services, representing the large community; the voluntary agencies; the relatives of persons who have been stricken by the disease. Yet we know that tuberculosis lurks within the population, often concealed in the bodies of the apparently healthy.

Case finding techniques have become mass approaches: chest x-ray film surveys of populations of cities or counties; tuberculin testing of school populations; tuberculin testing of entire counties.

The results have rarely lived up to the promise. Often they have not seemed to justify the tremendous advance organization and planning. Whatever the failure of these ventures in turning up active tuberculosis, they have been defended for their "plus" values: health education of the public; detection of heart disease or lung cancer; discovery of tuberculin reactors; facilitation of follow-up.

The mass approach and the advance planning and preparation do not allow these to be continuing programs, nor easily repeated. Hence we must be content with a single, thinly spread examination for possible tuberculosis.

One method of selecting individuals for examination resides in the tuberculin test. It is simple, easy of application, and has high reliability. Through it, the individual, his physician and the group interested in community health can learn who have been infected with the organisms of tuberculosis.

How to persuade the individual to seek examination without frightening him by untrue slogans; how to encourage him to be examined not just once, but annually or oftener has not yet been devised. How to keep physicians alert to finding tuberculosis, or entire medical societies sensitized to the problem is still to be worked out.

One possible approach—suggested by the late Dr. Hedberg in casual conversation—is the bounty plan.

Each community has an idea of the amount of money it spends annually for case finding. The cost for finding a single new tuberculosis patient has been quoted as from $500 to $800, when mass methods are used. Costs are proportionately higher in low prevalence areas.

The suggestion is now made that we offer this sum to any individual who turns up with previously unknown active pulmonary tuberculosis. Why not try this type of "bounty plan" in the counties where the new-case rate is low? The individual thus becomes responsible for initiating the examination and seeing that the results are properly reported.

The individual, moreover, may feel that he can "afford" to know whether

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he has tuberculosis if a sum of money can be assured to the family during his absence from home for treatment. A reference group will determine whether the criteria for active previously unknown tuberculosis have been met. The program is automatically continuing, is not a once over-lightly approach, and releases the voluntary staff from unrewarding duties.

Alternatively, why not offer to each county medical society $100 for each new case reported by its physicians? This may serve to encourage physicians to carry out intensive systematic search for tuberculosis in each patient who seeks medical attention.

The two plans may be set up competitively to test their relative effectiveness.

Where is the money coming from? From case-finding programs which might thus diminish in intensity as the bounty plan gains in popularity; from research grants, since this is definitely an untried procedure and can be set up as a project in comparative case-finding methods; from a beneficent government, if there is one, because tuberculosis treatment is a burden that is absorbed largely by the state; from a charitable foundation if one can be interested in trying a new method.

Certainly, tuberculosis case finding can be the responsibility of the individual potential patient, or the physician in the community. A fresh approach is in order. Assuredly, this is the time.

SECTION ON CARDIOVASCULAR DISEASES

Mitral Valve Surgery: Transventricular Valvuloplasty and Use of Ivalon Sponge Pack for Mitral Insufficiency†

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Since it became established that surgery can be of value in rheumatic valvular disease a wide variety of instruments and techniques have been devised for the relief of stenosis and incompetence of diseased mitral valves. None of these is universally accepted due to various shortcomings, the continuing search for more adequate methods, and the considerable variation in pathological findings which requires flexibility in the plan of surgical attack.

Undoubtedly every surgeon who has performed many mitral valvuloplasties has found that his results have improved with experience and with changes in the techniques that he employs. Bailey and co-authors[1] report that, after having performed over 1400 left-sided mitral commissurotomies, they had become "less and less satisfied with the procedure," largely because of difficulty in splitting or cutting the postero-medial commissure when this approach was used. Although most of the patients who have had surgery for mitral stenosis have been greatly improved, many have not derived maximum benefit from their operations. A surgeon's dissatisfaction is well justified when he has not been able to recover valve function to the greatest possible extent. In each instance he must strive for total relief of valvular and subvalvular stenosis and, when both leaflets have been mobilized as completely as possible, he must attempt to eliminate or reduce any insufficiency that exists.

Both fused commissures of some stenotic mitral valves can be split completely by finger fracture alone. These are not the valves that cause concern. It probably makes little difference whether they have been approached through a left posterolateral thoracotomy incision or through a left or right submammary incision. More often, one of the commissures splits readily and the other does not (generally the postero-medial when the left approach is used and probably the anterolateral when the right approach is used). It is well known that patients may be improved clinically when a single commissure has been split. For this reason, and be-

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cause use of a cutting instrument has sometimes produced serious valvular incompetence, surgeons frequently have made the decision to leave "well enough" alone after splitting only one of the commissures. In some instances the fibrous fusion of both commissures has been found to be so thick or so calcified that even commissurotomy with a knife has proved to be impossible and the surgeon has had to be content with simple finger dilatation of the valve. Even these patients may be temporarily improved; but, within months, their former symptoms return and become progressively worse.

With the passage of time it has become apparent that re-fusion of valve commissures occurs in a significant number of patients. Such re-fusion is most likely to occur when the fused commissures have been incompletely split at the initial operation, when subvalvular stenosis has not been recognized and relieved, or when extreme scarring and calcification have made mobilization of the leaflets impossible. With a valve that presents advanced fibrous stricture and subvalvular fusion, it is possible, as Bailey suggests, that the "stenosing process may continue to progress even though retarded by one or more operative procedures." If a valve has flexible leaflets, however, and good mobility is restored through surgery, it would seem improbable that re-fusion to any significant degree would occur unless there were a return of active rheumatic valvulitis.

We, like others,[2, 3] are convinced that for a satisfactory operation for mitral stenosis, commissural fusion must be eliminated completely and that, in a high proportion of patients, instrumental aids are required to accomplish this. Most widely used for cutting the commissures which resist finger fracture have been the guillotine type knives, first devised by Bailey. It requires considerable practice to manipulate these instruments satisfactorily and to cut accurately with them, when they are introduced into the left atrium beside the guiding finger. It seems that the surgeon using these knives, no matter how great his experience, will sometimes make a cut which veers from the line of the commissure and produces or increases valvular insufficiency. The same thing can happen with the Harken breadknife type of blade. This instrument is easier to guide and manipulate; but, when a thick commissure is encountered, it does not permit one to cut as forcefully as with the guillotine knife. The fingernail knife of Bakst, in our experience, permits much greater accuracy than either of the above, or any of the others that are passed through the atrium along the guiding finger. Until recently, we preferred it for those valves which resisted finger fracture. There are several other instruments that can be attached to the finger with a ring or as a thimble, which have similar advantages.

In 1954 DuBost[4, 5] reported use of a dilator introduced through the left atrial appendage for mitral valvuloplasty. Judging by the literature, this approach has not been widely used. At the annual meeting of the American College of Surgeons in 1956, Dr. Frank Gerbode mentioned introducing a dilator, similar to the Brock aortic valve dilator, through the wall of the left ventricle and using this to split the mitral valve commissures when fibrous fusion had been so severe as to resist fracture or cutting at a previous operation. According to a recent communication[6] he has used this technique five times (all re-operations) with one death. We have

also learned recently that Logan has used a similar technique for most of the operations for mitral stenosis that he has performed during the past four years.[7]

Since February, 1957, we have used the Brock dilator, passed through the left ventricle, with increasing frequency, not only in recurrent cases but in all cases where commissural fusion resists fracture by the finger alone. We find that the dilator, with amazing regularity, will not only split both commissures out to the annulus fibrosus but will also relieve the subvalvular stenosis which often co-exists. On three recent occasions we have encountered a fused anterolateral commissure which was so fibrous and thick that it would not split with the Brock dilator. In each instance we found that a Bailey commissurotomy knife, passed through the left ventricular stab wound, served to cut the resistant edge of the commissure. It seemed that such a cut could be made with much greater accuracy when the knife is passed through the ventricle, guided by the index finger in the left atrium, than when the knife is passed through the atrium beside the finger. On each occasion, after an initial cut with the knife, the remainder of the commissure was readily fractured either with the finger or with the dilator.

During the past year (November '56-'57) we have performed 64 mitral valvuloplasties. The dilator has been used in 38 of these. It has been used in 88 per cent of the mitral valvuloplasties performed during the last six months. In 9 per cent of the total group the dilator was being used for co-existent aortic stenosis and might, otherwise, not have been used for the mitral valve in all these. In the remaining, however, it is believed that the dilator contributed to more thorough and accurate splitting of the valve commissures than might have been accomplished by other available techniques. On several occasions, when extremely thick fibrous and/or calcific fusion was encountered, it seemed that only blunt force, such as that provided by the dilator, could have produced as satisfactory a result. Transventricular instrumentation has not appeared to increase the surgical risk and has seemed to reduce the likelihood of producing or increasing valvular insufficiency.

Unfortunately we are not as pleased with our means of surgically treating the regurgitation that often accompanies stenosis of the mitral valve, particularly that which presents as the dominant functional abnormality. Most of the operations that have been devised for mitral insufficiency have proved to be extremely unsatisfactory, either because the results were not lasting or because of the extremely high mortality that is associated with them.

At the 1956 meeting of the American College of Surgeons Harken discussed his use of an extrinsic baffle to reduce or eliminate the regurgitation that was found during operations for mitral stenosis. With the right index finger in the left atrium palpating the regurgitant jet, the surgeon may find that pressure on the posterior wall of the heart, with the middle finger of the same hand, will improve the competence of the valve without obstructing it. During the past year we have used a piece of Ivalon sponge under such circumstances, to replace the finger. Harken now uses a hard roll of gel-foam as the baffle. He considers the procedure a

good "strategic retreat" for mild insufficiency and has used it approximately two hundred times.[8]

At first we used the Ivalon sponge pack only in patients who were being operated upon primarily for mitral stenosis or mitral and aortic stenosis, the significance of the associated mitral regurgitation not always having been fully appreciated in advance. More recently we have used this sponge for a few patients in whom mitral regurgitation was known to be the primary problem. It is too early to evaluate the results in these patients, but clinical improvement has been evidenced by increased exercise tolerance, reduction in need for diuresis and progressive decrease in heart size.

One must admit that this seems like a rather primitive type of operation. For those patients who have a widely dilated valve ring, circumferential purse-stringing as reported by Glover[9] and others, polar cross-fusion of the annulus fibrosus by either a closed (Nichols[10]) or an open (Lillehei[11]) technique, or using some type of intracardiac prosthesis (Rumel[12]) are likely to prove superior. For those patients whose regurgitation is due to scarring, retraction and contraction of a valve leaflet, the sponge pack appears not only to be safer and simpler, but also less likely to produce stenosis or to interfere with valve function.

Technique

The patient is placed on the operating table in the supine position. Following induction of anesthesia and intubation the left side of the body is raised to almost a 45° angle and the left arm is supported overhead.

A left submammary incision is used and is carried through either the 4th or 5th intercostal space, depending on the size of the heart and the relative positions of the left atrial appendage and the apex of the heart, as determined by x-ray. It has rarely been necessary to divide a costal cartilage, although costochondral separation or rib fracture sometimes occurs as a result of spreading the ribs. The pericardium is incised from the apex of the heart to well up over the pulmonary artery, in front of the phrenic nerve. The pericardial edges are retracted with stay sutures and a small window is made in the posterior pericardium to improve drainage from the pericardial sac into the pleural cavity both during and after surgery. The cardiac chambers and great vessels are evaluated by inspection and palpation, noting the presence of thrills. Direct pressure determinations within the structures are not obtained routinely unless aortic valve disease is present. If it is, a cardiac catheter is passed through a tiny stab wound in the apex of the left ventricle up into the aorta and a record is made of the pressure gradient across the aortic valve. When it is difficult to pass a catheter through a stenotic aortic valve, needles attached to the strain gauge are introduced directly into the left ventricle and aorta in order to determine the pressure gradient. After an aortic valve has been dilated the pressures are again determined in the same manner.

If the left auricular appendage is large, we do not routinely place a purse-string suture around it. If it is small, if it obviously contains a thrombus, or if it has been amputated at a previous operation, a purse-string suture is always placed around the base of the appendage or that

area of the atrial wall through which the finger will be introduced. The ends of the purse-string suture are then threaded through a Rumel tourniquet. A Glover clamp on the left atrial appendage controls bleeding while the incision is being made or whenever the incision is not plugged with a finger. The right index finger is used for intracardiac digital exploration.

If it is decided that the Brock dilator will be used for the aortic valve, the mitral valve, or both, a small stab wound is made in the middle of an avascular area near the apex of the left ventricle. Here, again, a purse-string suture is not always used. If the left ventricle is dilated and its musculature lacks tone, three stitches of no. 2 Anacap are placed around the selected area and the ends of the suture are threaded through a Rumel tourniquet. More often a simple mattress suture of no. 00 atraumatic Deknatel is placed around this area, without use of the tourniquet. Traction on this helps to expose the site of the incision and steadies the heart. It also helps to control bleeding from the incision. A stab wound made with a no. 44 Beaver blade, thrust obliquely upward, is of adequate size. It is smaller than the dilator, but that is desirable. The dilator stretches the opening without tearing the muscle and, while in place, it fits snugly so that there will be little if any bleeding around it (Fig. 1).

If aortic valvuloplasty is to be performed the index finger in the left atrium and the adjoining thumb, externally, identify the position of the valve which frequently is calcified. The dilator, passed along the outflow tract of the left ventricle can readily be guided into the orifice of the aortic valve between thumb and finger.

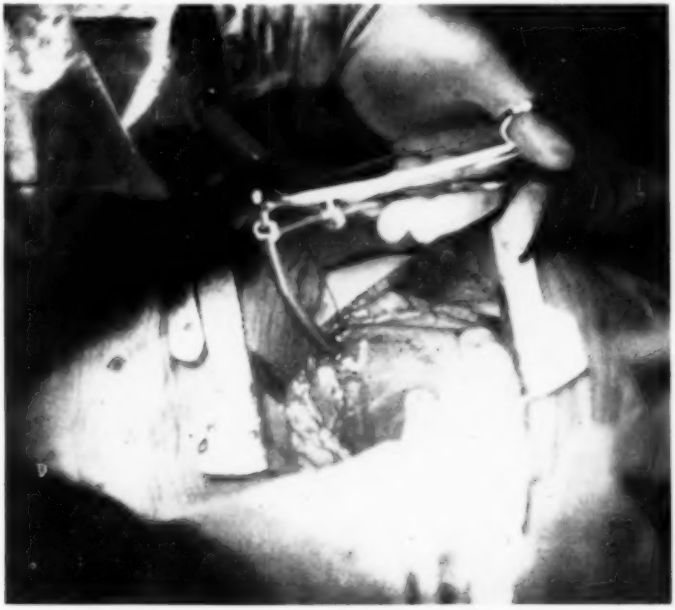

FIGURE 1: The Brock dilator has been inserted through the apex of the left ventricle into the orifice of the mitral valve. The operator's index finger guides it into place from within the left atrium.

In the case of mitral valvuloplasty the Brock dilator is guided by the intracardiac finger between papillary muscles and chordae tendinae into the orifice of the valve. Here the dilator is opened one or more times until the commissures are completely split or it is determined that no further splitting can be accomplished. The Brock dilator is not ideal for this maneuver. Its bars do not spread far enough for most valves and it tends to slip out of the valve because the surfaces of the bars are so smooth and there is not quite enough curve to the handle. Recently we have obtained a larger dilator with notched bars (Fig. 2). The Brock dilator, however, has served well. When it does not split both commissures completely the remainder of the splitting can generally be accomplished either with finger dissection or by opening the dilator again with the finger in one of the commissures for counterpressure. Subvalvular stenosis seems to be relieved very well when the dilator is opened in the inflow tract of the left ventricle.

If there is very thick commissural fusion which fails to split with the dilator, this instrument is removed and replaced with a Bailey commissurotomy knife, passed through the same ventricular stab wound. The knife, guided by the intracardiac finger into the mitral valve orifice, is opened inside the heart and hooked over the commissure in question. With instrument and finger approaching the commissure from opposite directions, using the two hands, it is felt that knife can be positioned much more accurately than when the instrument is guided along the finger through the atrium, since one has much more kinesthetic sense added to the cutaneous sense of the finger tip and the instrument and finger do not have to be moved and positioned as a unit.

Bleeding from the ventricular stab wound is sometimes vigorous but is

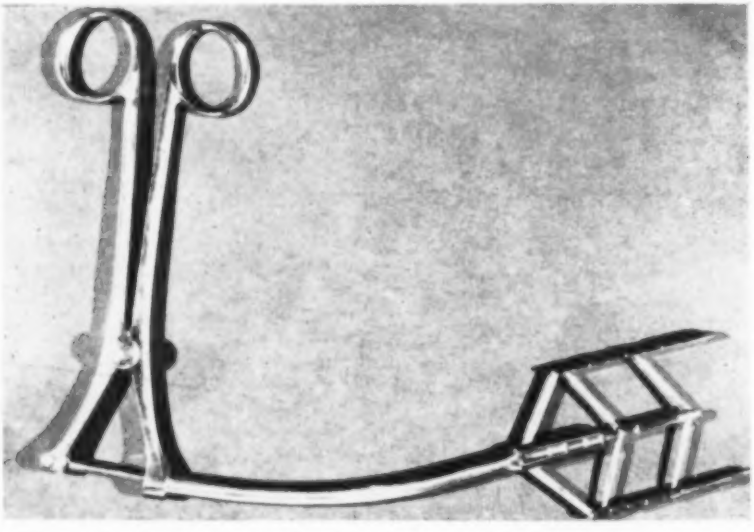

FIGURE 2: This large size modification of the Brock dilator was made for us by George Pilling & Son Company. The bars, which have a spread of two inches, are inconveniently long. It is intended to shorten them at their distal ends. On a few occasions, this large dilator has seemed mandatory for a satisfactory valvuloplasty.

generally controlled with ease by finger pressure while two or more small, interrupted stitches of no. 00 atraumatic Deknatel are placed across it. Surprisingly, bleeding from this small stab wound may stop spontaneously, without sutures, after pressure has been applied for a while, particularly if the myocardium is thick and has good tone. However, we have always considered it advisable to place the sutures. Sometimes bleeding is more difficult to control and it may prove desirable to purse-string the area and control bleeding with this while additional interrupted or mattress sutures are placed. We have considered brief plugging of the stab wound from within, with the intracardiac finger, as a possible recourse. When we used the large Bailey dilator for aortic valve surgery we sometimes found it useful to control ventricular bleeding by sewing a plug of skeletal muscle into the stab wound. With the smaller Brock dilator this has not yet been necessary.

Placement of an Ivalon sponge pack is carried out in the following manner: After any existing stenosis has been relieved and the valve leaflets have been mobilized as fully as possible the degree of mitral regurgitation is estimated by the intracardiac right index finger. Pressure with the adjoining middle finger on the posterior aspect of the heart determines the site at which pressure should be applied in order to obtain maximum reduction or elimination of the regurgitant jet. At first it was thought that one should simply push the mural leaflet portion of the mitral annulus forward so that the leaflets could be better apposed during ventricular systole. Experience indicates, however, that sometimes, especially when the mural leaflet has lost much of its substance, it may be more effective to push the left ventricular wall forward so that the septal leaflet will flap against it or to put a large pack against the redundant left atrial wall pushing part of the latter down as a replacement for the mural leaflet.

The packs have varied greatly in size. Some have had to be disturbingly large. Most have been about 4 x 4 x 8 cm., with the edges rounded. This pack is simply placed in the selected position, in the axis of the A-V sulcus, replacing the middle finger on the posterior aspect of the heart. It is easier to place the pack if the left index finger is introduced into the atrium, in place of the right, particularly if the pack is large, but this is generally not necessary. In any case a finger is kept in the left atrium during positioning of the sponge to determine when maximum reduction in regurgitation has been achieved. We, like Harken, have not found it necessary to suture the pack into place. Anatomical barriers and the pericardium, pulled tightly over the pack, seem to hold it in the selected position.

The rest of the procedure, including such things as the management of thrombi encountered in the left atrium, follows standard lines and need not be discussed here.

Results

From November 1, 1956 to November 1, 1957, we performed 64 operations for mitral valvular disease.

Mitral Stenosis

Thirty four of the operations were for "pure" mitral stenosis and the Brock dilator was used in 21 (62 per cent) of these. There have been

no deaths in this group and improvement has been good in all, excellent in most. It is difficult to compare the 21 patients in whom the Brock dilator was used with the 13 in which it was not used, since the valves in all but one of the latter split adequately with finger fracture alone. Actually only six of the latter were operated upon since our first experience with the Brock dilator for the mitral valve (February, 1957). The most obvious difference between the two groups is that when the dilator has not been used there has frequently been little or no change in the cardiac murmurs as a result of the surgery. When the dilator was used there was marked reduction or abolishment of the apical diastolic murmur in every case (Fig. 3). It is also of interest that appearance or increase of a regurgitant jet was noted more frequently by the surgeon after finger fracture than after use of the dilator. We have not done routine pre- and post-operative left heart catheterizations for pressure curves and gradients across the mitral valve.

Multiple Valvular Disease

The Brock dilator was used for relief of mitral stenosis in 9 additional patients who also had mitral regurgitation of significant degree for which Ivalon sponge packs were used. One of these patients died suddenly 5 weeks following his operation. He was a 39-year-old man who had shown initial improvement following finger fracture of a calcified stenotic and incompetent valve 2 years previously. In chronic congestive failure, with findings of mitral stenosis, mitral insufficiency and tricuspid insufficiency, he appeared to be in the terminal stage of rheumatic heart disease when he expressed strong desire for the operation which was directed

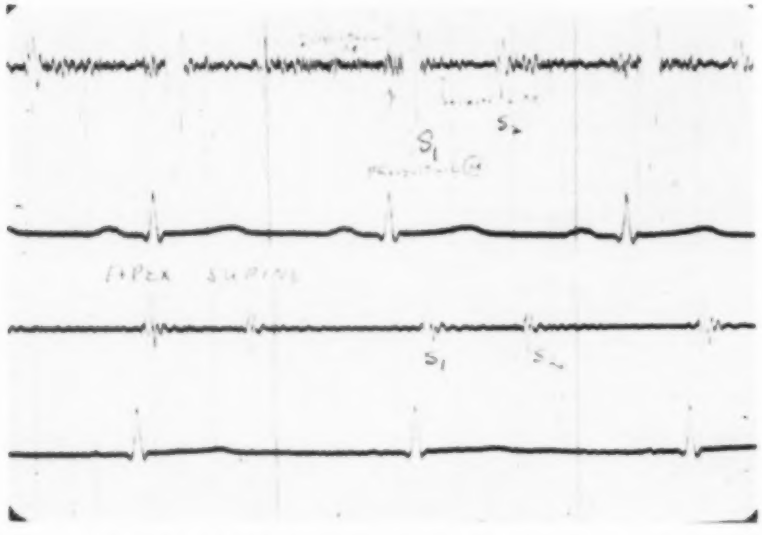

FIGURE 3: The high fidelity phonocardiograms show the marked reduction of the apical diastolic murmur in a patient with mitral stenosis following transventricular mitral valvuloplasty with the Brock dilator. The upper tracing was obtained preoperatively, the lower tracing post-operatively. (Courtesy of Dr. Leonard Rose.)

primarily towards relieving the severe mitral incompetence rather than eliminating the residual stenosis. It was considered that valve function was definitely improved by the operation and following it his anascarca was effectively controlled, this having been impossible before surgery. The cause of death was not determined at autopsy. In the eight surviving patients moderate to marked improvement was obtained.

The Brock dilator was used to relieve stenosis of both the aortic and mitral valves in 4 patients with bivalvular disease. One of these patients died in acute failure 5 days following the operation. The other three have been greatly improved.

In 4 more patients who had "significant" mitral regurgitation as well as aortic and mitral stenosis the Brock dilator was used for both valves and Ivalon sponge packs were placed. One of these died with multiple cerebral emboli and terminal pneumonia on the 3d post-operative day. Another died 3 months post-operatively, following initial improvement. The other two patients showed marked improvement.

Two patients with mitral and aortic stenosis had the Brock dilator used for the aortic valve; but, following finger fracture of the mitral valve, the commissures were adequately split and no resistance was encountered when the dilator was opened in this valve. Both these patients have done well.

Mitral Insufficiency

It is clearly recognized that these preliminary results for mitral insufficiency do not provide a firm basis for long range prognosis. They are presented to help illustrate a simple, low risk procedure which we believe to be useful, at least until better techniques are established.

An Ivalon sponge pack has been used for mitral regurgitation in 23 patients. There was associated mitral, or mitral and aortic, stenosis in 20 of these. In most the regurgitation, alone, would not have been considered an indication for surgery and the presence of significant regurgi-

FIGURE 4: These pre-operative (left) and six months post-operative (right) roentgenograms demonstrate reduction in heart size after placement of an Ivalon sponge pack for relief of severe mitral valve insufficiency.

tation, not always fully appreciated in advance, was considered an indication for the pack when the patients were being operated upon, primarily, for their stenotic lesions. After the pack had appeared to improve valve function in several such patients it was used for severe mitral regurgitation without stenosis. It has been used only three times under such circumstances and one of these patients, who developed reversible ventricular fibrillation during the operation, died on the 3d post-operative day with multiple pulmonary emboli. While it is too early to evaluate the results in the other two patients completely, both have been benefited thus far, six and eight months following their operations. They both required mercurial diuretics two to three times a week prior to their operations and have not required them since. There has been decrease in heart size in both (Fig. 4), and exercise tolerance has been improved moderately in one and markedly in the other.

On one occasion we felt that a sponge pack was obstructing the mitral valve excessively and so did not leave it in place. (This patient had marked calcification and fixation of both valve leaflets even after the commissures had been completely split.) It is believed that no operation, short of complete prosthetic replacement of the valve, could have eliminated the regurgitation without obstructing blood flow excessively.

SUMMARY

Some of the techniques applicable to mitral valve surgery have been reviewed and the need for flexibility of approach and improvement in methods emphasized. The techniques reported here are not original with us but derive from reports previously made by Dr. Frank Gerbode and Dr. Dwight Harken.

Surgical experiences from November, 1956, to November, 1957, in 64 cases of mitral valvular disease have been presented. Results, while favorable, are early and evaluation therefore must be guarded. Valvular stenosis resisting finger fracture has responded uniformly well to transventricular use of the Brock dilator. Murmurs have been greatly reduced or eliminated.

Patients with mitral regurgitation complicating other valvular disease have had their regurgitation reduced or eliminated with use of an intrapericardial Ivalon sponge pack. Gratifying improvement has been seen in two of three patients with severe "isolated" mitral insufficiency.

RESUMEN

Después de revisar algunas de las técnicas que se usan en la cirugía de la válvula mitral, se hace notar que se requiere flexibilidad y mejoría al aplicar los métodos. Las técnicas aquí referidas no son originales nuestras, sino que derivan de informaciones hechas antes por los Dres. Frank Gerbode y Dwight Harken.

La experiencia clínica desde Noviembre de 1956 hasta Noviembre de 1957, en 65 casos de enfermedad de la válvula mitral son el objeto de esta comunicación. Los resultados aunque favorables son recientes y su valuación por consecuencia está sujeta a reserva.

La estenosis valvular que resiste a la fractura por la maniobra digital ha respondido bien con constancia al uso del dilatador transventricular de Brock. Los murmullos se han reducido grandemente o se han eliminado.

En los enfermos que han tenido regurgitación mitral como complicación de otras enfermedades valvulares se ha logrado la disminución o desaparición de esa regurgitación por el uso de empaque intrapericárdico de esponja de Ivalón. Se ha observado una satisfactoria mejoría en dos de tres enfermos de insuficiencia mitral "aislada."

RESUME

Quelques-unes des techniques applicables à la chirurgie de la valvule mitrale sont passées en revue, l'accent mis sur la nécessité de la flexibilité des appareils d'approche, et l'amélioration des méthodes. Les techniques rapportées ici ne sont pas originales, mais dérivent de communications faites antérieurement par le Dr. Frank Gerbode, et le Dr. Dwight Harken.

Les auteurs rapportent leur expérience chirurgicale qui, de Novembre 1956 à Novembre 1957, porte sur 65 cas d'affections de la valvule mitrale. Les résultats, bien que favorables sont trop récents et l'estimation par suite ne peut être garantie. La sténose valvulaire résistant à la rupture digitale a toujours bien répondu à l'emploi transventriculaire du dilatateur de Brock. Les soufles ont été grandement réduits ou éliminés.

Les malades atteints de régurgitation mitrale, compliquant d'autres affections valvulaires ont eu leur régurgitation réduite ou éliminée avec l'emploi d'un tampon d'éponge d'Ivalon intrapéricardique. Une amélioration considérable a été constatée chez deux des trois malades atteints d'insuffisance mitrale grave "isolée."

ZUSAMMENFASSUNG

Es wurden einige der Operationsverfahren, die bei der chirurgischen Behandlung der Mitralklappe angewandt werden können, besprochen und die Notwendigkeit einer Anpassungsfähigkeit des Vorgehens und eine Verbesserung in den Methoden betont. Die wiedergegebenen Verfahren stammen im Original nicht von uns, sondern aus zuvor gegebenen Berichten von Dr. Frank Gerbode und Dr. Dwight Harken.

Es wurden chirurgische Erfahrungen vom Nov. 1956 bis Nov. 1957 an 65 Fällen von Mitralklappenerkrankung vorgelegt. Es handelt sich obwohl um günstige, so doch um frühe Ergebnisse, und ihre Auswertung muss daher mit Sorgfalt erfolgen. Eine der Sprengung mit dem Finger widerstehende Klappenstenose hat in jedem Fall günstig auf die transventrikuläre Anwendung des Brock'schen Dilatators angesprochen. Geräusche wurden wesentlich verringert oder beseitigt.

Patienten mit mitralem Rückstrom als Komplikation anderer Klappenerkrankungen erfuhren eine Verringerung des Rückstromes oder dessen Beseitigung durch Benutzung eines intraperikardialen Ivalon-Schwammstückes. Eine erfreuliche Besserung sah man bei 2 von 3 Kranken mit isolierter schwerer Mitralinsuffizienz.

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Clinical Dyspnea and Cardiopulmonary Function Studies

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The correct appraisal of the symptom dyspnea, in any given patient, is still primarily based on a good clinical and radiological study. Nevertheless, this basic approach cannot, in many cases, provide a full understanding of the physiopathology of dyspnea and still less measure it quantitatively. Moreover, in some circumstances, it is beyond the pure clinical approach to detect malingerers or to eliminate dyspnea based on purely emotional disturbances. From the therapeutic point of view, the early correct diagnosis may be lifesaving, and there is an increasing demand on the functional laboratory to provide a rapid and more accurate diagnosis. A battery of laboratory tests to interpret cardiopulmonary disturbances has come into common use.[1] Inspired by previous workers we have utilized the findings of some of them in the hope of understanding the basic disturbances leading to dyspnea.[2, 3] Our purpose is to show that the judicious use of a limited number of tests may be enough to throw light on the derangement. We shall also mention the therapy in some of the cases where it has a bearing on the subject.

Dyspnea of Cardiac Origin

Case 1. Dyspnea of insufficient cardiac output. A 24 year old woman with objective signs of mild mitral stenosis complained of dyspnea on effort. Her general condition was good. X-ray film of the chest disclosed only slight cardiac enlargement compatible with mitral stenosis and no signs of intrinsic lung disease.

Her pulmonary function studies (Fig. 1) showed essentially normal values apart from a slight diminution of the maximum breathing capacity. No hyperventilation was present at rest and the response to exercise was normal. The breathing reserve at rest and during standard exercise was within normal limits. There was no sign of bronchial constriction. Her cardiac output at rest and during exercise showed normal values, but a marked increase in the A-V oxygen difference was noted during exercise. This finding is in keeping with an insufficient increase of cardiac output during exercise and is an early pointer to "occult" forward failure.

The dyspnea in this case is related (a) to an increased cost of breathing during exercise;[4] (b) to the slight degree of forward failure, this leading to poor tissue and muscular oxygenation, therefore producing awareness of "dyspnea" as a manifestation of muscular fatigue,[5] and (c) to the diminished oxygen saturation of mixed venous blood.[6]

Case 2. Dyspnea of insufficient cardiac output and irreversible pulmonary hypertension. A 27 year old man with advanced signs of mitral stenosis presented moderate cardiac enlargement and marked vascular engorgement of the lungs. The electrocardiogram was consistent with right ventricular hypertrophy and strain. A technically adequate mitral valvotomy was performed. After operation his condition did not improve and continued to be marked by exertional dyspnea and mild chronic congestive heart failure. Figure 2 presents the laboratory findings.

The pulmonary function tests before and after operation were essentially the same. (Figure 3 shows the results after operation.) It can be seen that he is hyperventilating at rest and after a standard exercise this hyperventilation increases considerably and along with it, the dyspnea. The MBC and V.C. are still quite normal. There was no sign of bronchial obstruction. Cardiac catheterization data, before and after operation, throws some light on the mechanism of his dyspnea. Valvotomy increased his resting cardiac output though to an insufficient degree. During exercise, cardiac output failed to increase and actually decreases because of myocardial damage. But the striking feature is the irreversible pulmonary artery hypertension arising as a result of the

With the technical assistance of F. Katz.

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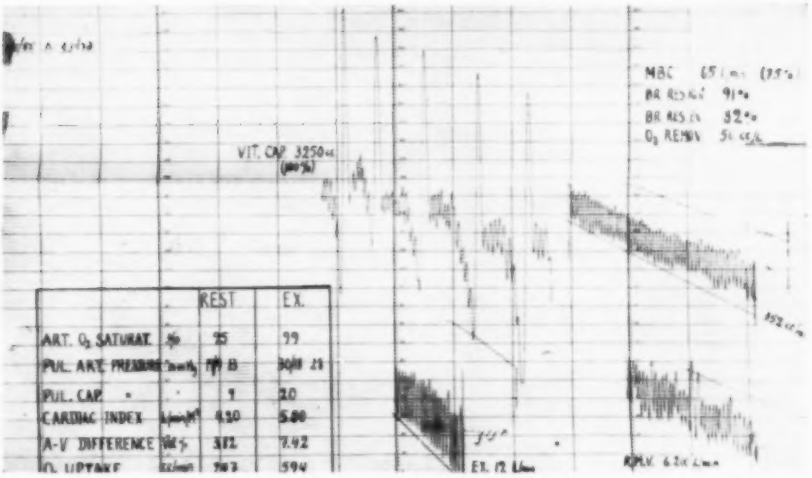

FIGURE 1

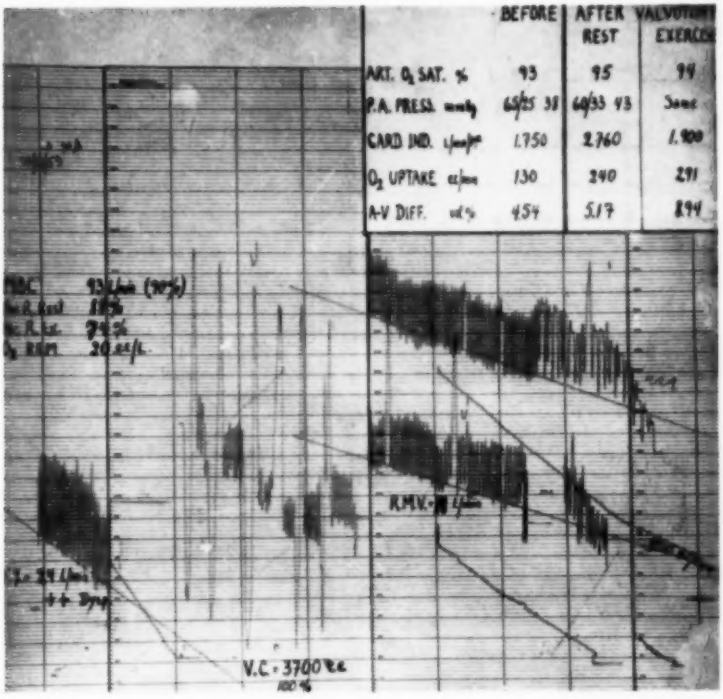
BEFORE
AFTER REST
VALVOTOMY EXERCISE
ART. O2 SAT. % 93 95 99
P.A. PRESS. 65/25 38 60/33 43
CARD. IND. 1.750 2.760 1.900
O2 UPTAKE 130 240 291
A-V DIFF. 4.54 5.17 8.94
V.C. - 3700 cc

FIGURE 2

extensive pulmonary arteriolosclerosis.[6] (Demonstrated in the lung biopsy taken at the time of operation.)

Hyperventilation and dyspnea in this case are due to a twofold mechanism: at rest they are primarily a function of the permanently increased cost of breathing of a rigid lung, which is due in turn to extensive pulmonary artery changes. On exercise dyspnea was intensified by the insufficient increase of cardiac output.[1, 7] Reduced arterial oxygen saturation was an added factor producing dyspnea by its accentuation of pulmonary artery hypertension.[8]

Case 3. Dyspnea of reversible pulmonary hypertension. A 16 year old boy whose main complaint was centered around dyspnea of eight months' duration was found to have mitral stenosis. There was no sign of overt cardiac failure. Because of the rapidly progressing symptoms and electrocardiographic signs of right ventricular strain, it was decided to operate on him.

Figure 3 shows his pulmonary function before operation. (There was no change after the operation.) The values are still within normal limits. The diminished V.C., in the absence of bronchial obstruction or other signs of pulmonary insufficiency, is probably due to lack of cooperation. A proof of that is the normal value for the MBC performance. The cause of the dyspnea can be found in the cardiac catheterisation data. The only abnormal finding before operation was a considerable increase in pulmonary artery pressure; the cardiac output was within normal limits. After operation the cardiac output was unchanged, but the striking reduction of pulmonary artery pressure was followed by disappearance of the dyspnea.

Obviously in this case the dyspnea was related to increased lung rigidity due to pulmonary hypertension which calls for an increased cost of breathing. The improvement in this patient after valvotomy shows that in the natural history of mitral stenosis the dyspnea of pulmonary hypertension is not necessarily irreversible. We have pointed out[9] that in the functional classification of mitral stenosis there is a special group of patients in the young age, clinically group II, characterized by almost normal heart size, ECG marked signs of right ventricular strain, and pulmonary hypertension, in whom the rapidly progressing symptoms are not necessarily related to decreased cardiac output. In this group the dyspnea may be readily relieved after valvotomy when it is followed by a striking fall in pulmonary artery pressure.

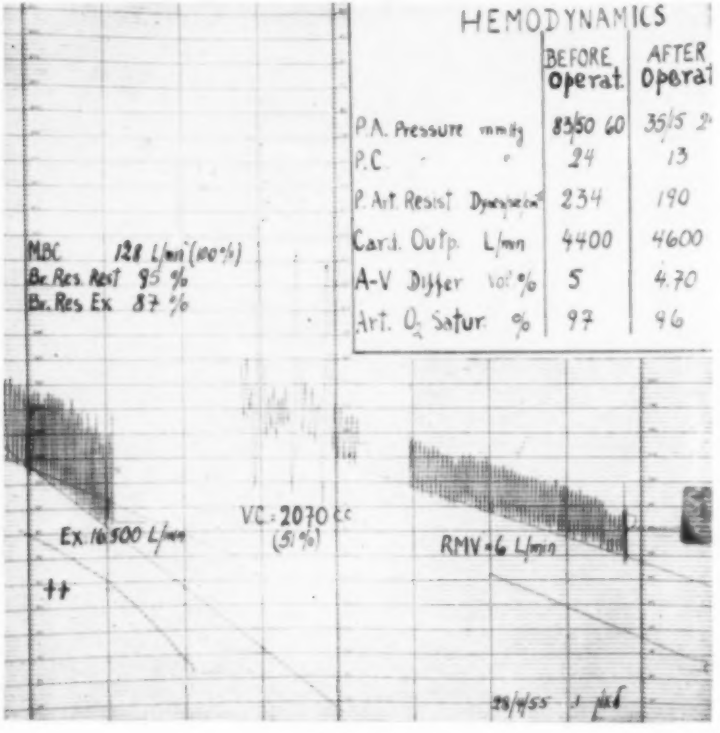

FIGURE 3

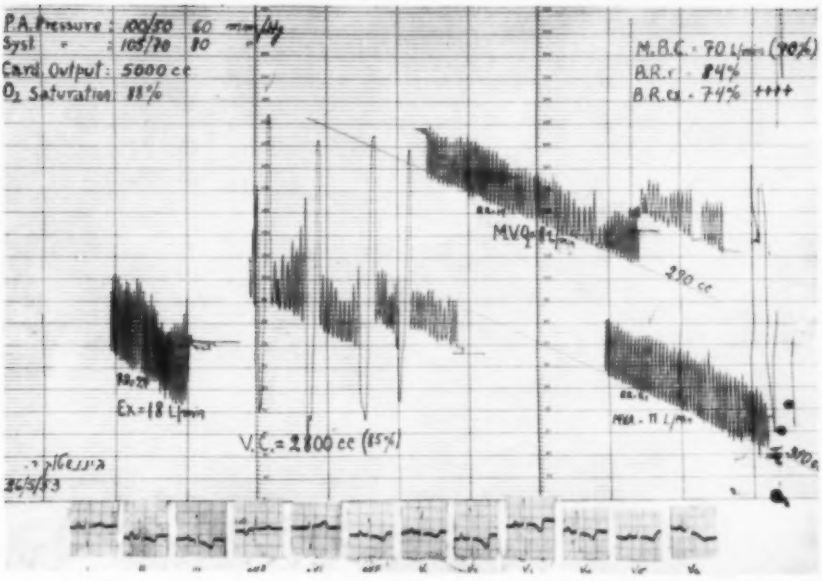

FIGURE 4

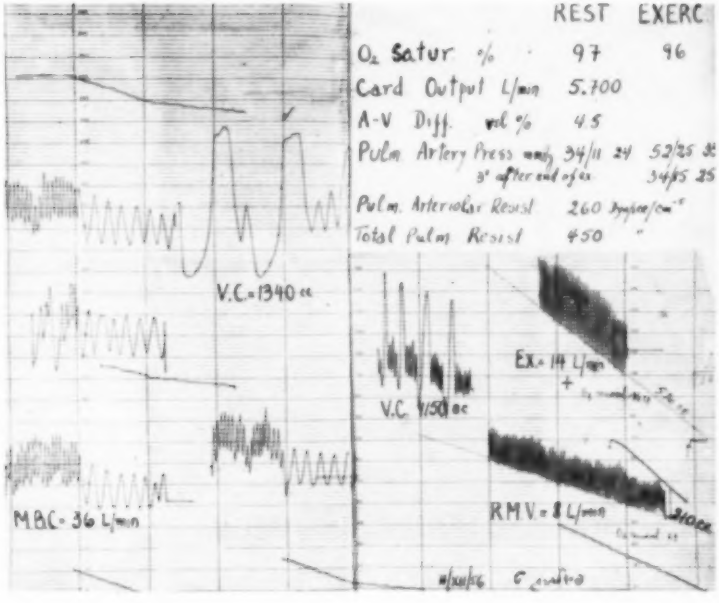
REST EXERC
O2 Satur % 97 96
Card Output L/min 5.700
A-V Diff. vol % 4.5
Pulm Artery Press mm Hg 34/11 24 52/25 3
3' after end of ex 34/15 25
Pulm. Arteriolar Resist 260 dynes/cm
Total Pulm Resist 450
V.C. = 1340 cc
M.B.C. - 36 L/min
V.C. 1/50 cc
Ex - 14 L/min
RMV - 8 L/min

FIGURE 5

The preceding cases have shown that ventilatory function studies are by themselves of little help in explaining the dyspnea of rheumatic heart disease. We have studied this aspect and found that beside the diminution of MBC and breathing reserve at exercise the other values of pulmonary ventilation do not accurately reflect the functional derangement in these patients.[10]

Case 4. Dyspnea of progressive primary pulmonary hypertension. A 22 year old woman, whose symptoms started six months before admission to the hospital was bedridden by dyspnea which in a short time was followed by cyanosis, intractable heart failure and death. Her ECG showed marked right ventricular hypertrophy and strain. At the time of this study heart failure was not yet conspicuous.

Figure 4 shows tachypnea and hyperventilation at rest and during slight exercise. There was no clear-cut sign of restrictive or obstructive pulmonary insufficiency. On the other hand, the picture is dominated by severe pulmonary arterial hypertension of the same magnitude as her systemic blood pressure,[11] *but without a decrease of cardiac output.* The chemical factor, oxygen unsaturation, already present, helps to sustain pulmonary hypertension and also serves as an accessory stimulus for hyperventilation and dyspnea. We could not find any sign of an intracardiac or intrapulmonary shunt to explain the decreased oxygen saturation of the blood.

Dyspnea in this case is primarily due to increased lung rigidity leading to increased ventilatory effort. This seems to be triggered by the pulmonary hypertension stimulating nerve endings in the pulmonary artery.

The Dyspnea of Bronchopulmonary Origin

This type of dyspnea is usually detected easily by clinical and radiological means. However, pulmonary function tests contribute to the understanding of the physiopathological steps leading to dyspnea. The help given by new technics for the investigation of the elastic and non-elastic respiratory chest resistances have provided a most useful approach to the study of the cost of breathing.[12] A quantitative estimate of the work of breathing still

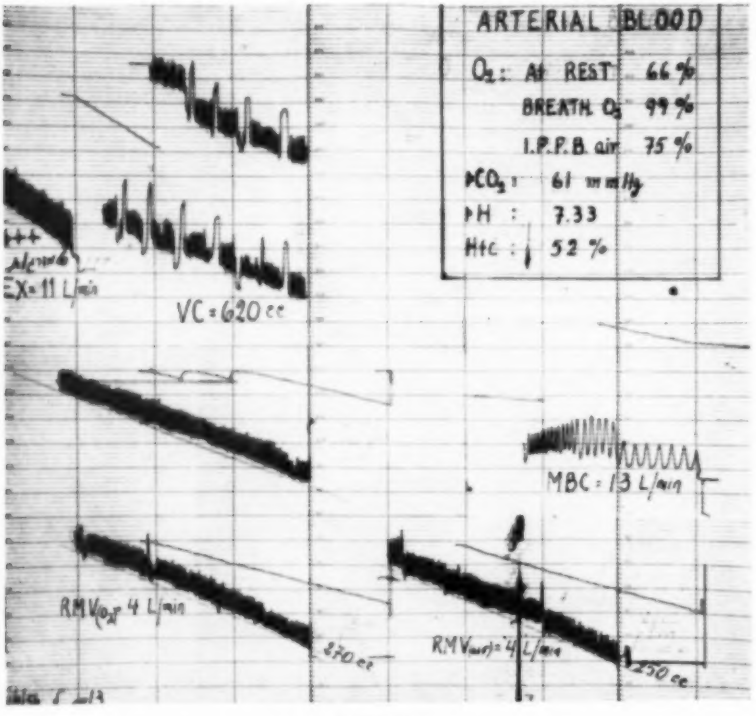

FIGURE 6

does not solve the problem of the measurement of dyspnea, but it represents the best method by which we can follow its changes. Nevertheless, it is possible by the use of simpler tests to understand the dyspnea of broncho-pulmonary origin.

Case 5. Transient dyspnea due to reversible pulmonary hypertension in a single functioning lung. A 54 year old woman who had active pulmonary tuberculosis 20 years ago had left pneumothorax instituted and discontinued after two years because of adhesions and pleural effusion. Afterward a left phrenic nerve crush was performed. For the last 15 years the disease has been quiescent and the sputum free of bacilli. Radiologically a consistent homogeneous shadow was seen over the entire left lung field. Recent bronchography and tomography showed an incomplete stop in the main left bronchus. No sign of malignancy was found. For the last 10 years she has been experiencing slight dyspnea on effort of a non-progressive nature.

Her pulmonary function studies (Fig. 5) showed an almost parallel decrease of V.C. and MBC values, with only slight evidence of bronchial obstruction. There was no hyperventilation at rest, and the response to exercise was normal. Arterial oxygen saturation was normal at rest and after exercise. These values are quantitatively consistent with the functional performance of a person of her age, height and weight breathing with only one lung. The hemodynamic data at rest showed a normal cardiac output and A-V Oxygen difference, and a slight increase of pulmonary artery pressure. The latter increased clearly on exercise but promptly returned to the previous level. Because of persistent empyema extrapleural pneumonectomy was performed and the excised lung was found to be completely airless thus corroborating the preoperative functional diagnosis.

Considering all the data one might say that at rest the single functioning lung was able to provide essentially normal ventilation and gas exchange, the circulation proceeding normally and therefore no dyspnea was present. At exercise, ventilation and gas exchange were still within normal limits, but the transient increase of pulmonary artery pressure increases the breathing effort and slight dyspnea supervenes. This is practically a constant finding after pneumonectomy and applies equally well to the single functioning lung of our patient.

Case 6. Dyspnea of restricted chest motion. A 56 year old woman with kyphoscoliosis since childhood, who had progressively incapacitating dyspnea for the last five years accompanied by intense cyanosis had an enlarged liver without peripheral edema. The extent of her chest cage deformity was marked.

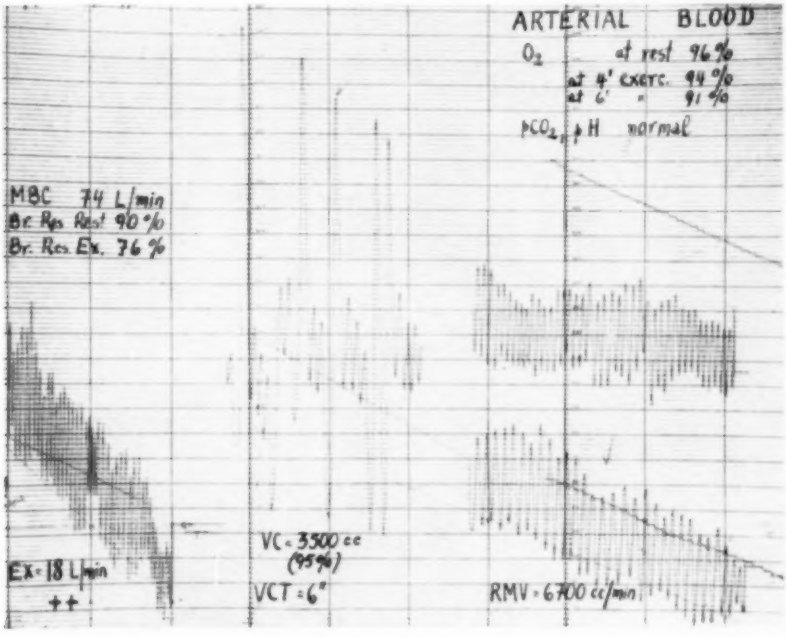

FIGURE 7

Her pulmonary function studies (Fig. 6) showed marked signs of restrictive pulmonary insufficiency. Despite her increased breathing effort and tachypnea she was actually hypoventilating (only 4 liters per minute). An exercise trial was immediately discontinued because of incapacitating dyspnea.

The arterial blood values showed marked oxygen unsaturation, increased pCO_2 and respiratory acidosis. No sign of arterio-venous shunt was present as demonstrated by her response to 100 per cent oxygen breathing. The chronological development of her dyspnea may be explained as follows: restriction of thoracic cage motion, producing tachypnea and increased breathing effort. Pulmonary insufficiency was thus compensated for years at the cost of more breathing work. When hyperventilation was no more effective, hypoxia first and then CO_2 retention and acidosis set in, adding then a chemical factor to further accentuate her dyspnea. With the passage of time also the chemical stimulus was no longer effective to stimulate hyperventilation. This last stage is characterized by hypoventilation and also marked by the development of cor pulmonale as a result of increased pulmonary artery pressure which in turn also helps to trigger dyspnea.

We instituted pneumoperitoneum and to our surprise after several "refills" she was able to get out of bed, do some walking and light home chores. No clear cut change was seen in the control ventilation studies, but her oxygen saturation went up to 89 per cent and the signs of heart failure subsided. This was probably brought about by an improvement in intrapulmonary mixing which ameliorated the chemical factor contributory to her dyspnea and produced a drop in the increased pulmonary artery pressure.

Case 7. Dyspnea of pulmonary fibrosis. A 44 year old man who for the last 20 years had worked in a metal work factory complained of progressive dyspnea on exertion. The physical examination of the heart and lungs was negative. The chest x-ray film showed a decided increase of pulmonary markings throughout both lung fields without signs of emphysema.

The ventilation and gas exchange at rest were normal without signs of restrictive or obstructive insufficiency. (Fig. 7) At exercise, along with the sensation of dyspnea appears a disproportionate hyperventilation. At the same time arterial oxygen saturation decreases. This type of response is consistent with pulmonary fibrosis, which also includes the alveolo capillary membrane.[11] His dyspnea was brought about by the increasing breathing effort to overcome the barrier of diffusion when exercising. This barrier represents a stimulus for hyperventilation. The hypoxia at exercise represents an added stimulus in the hyperventilation drive and dyspnea.

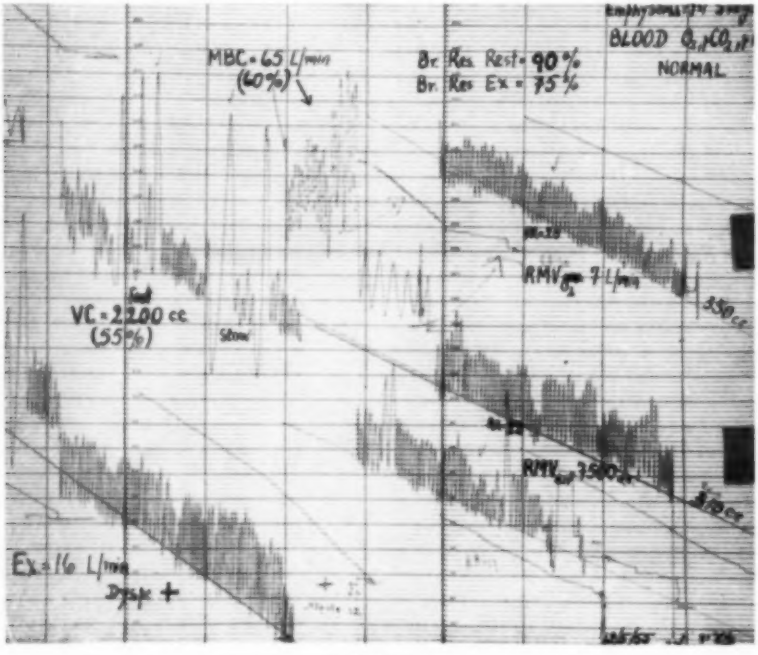

FIGURE 8

Dyspnea of emphysema.

The development of chronic pulmonary emphysema is marked by stages, which despite their overlapping, follow a certain pattern.[14, 15] By the same token, dyspnea is provoked and maintained by different factors acting alone or in combination.

Case 8. First stage of emphysema. A 33 year old man with a 10 year history of asthmatic attacks was free from active asthma when he was investigated. The x-ray films of the lungs showed increased translucency and the diaphragmatic excursions

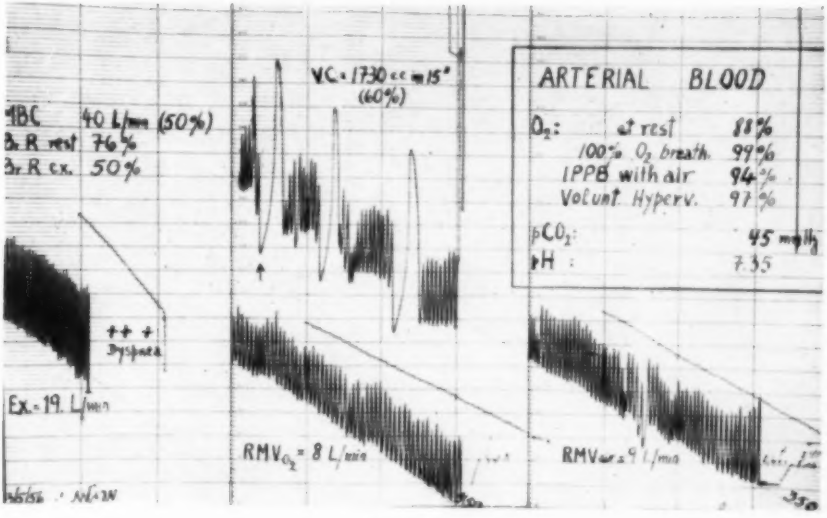

FIGURE 9

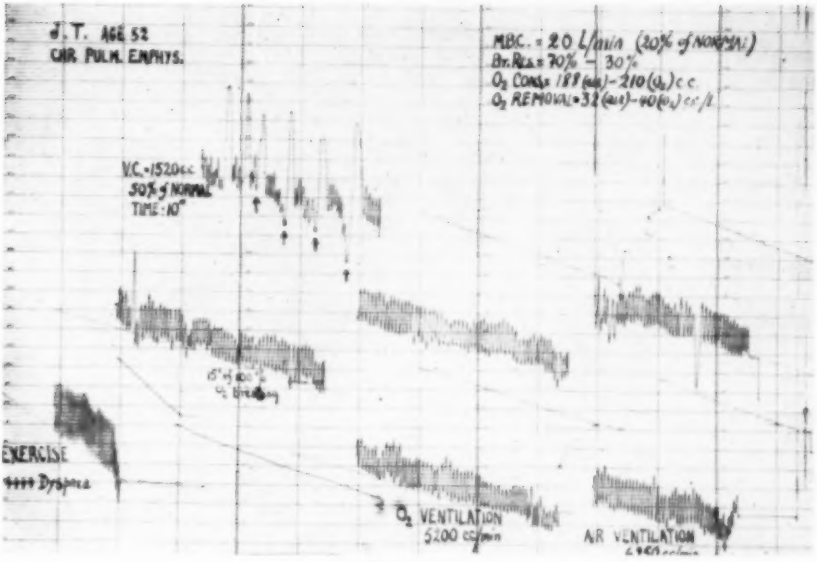
J. T. AGE 52
CAR. PULM. EMPHYS.
MBC. = 20 L/min (30% of NORMAL)
Br. Res = 70% – 30%
O2 Cons = 189 (air) – 210 (O2) cc
O2 REMOVAL = 32 (air) – 40 (O2) cc/l
VC. = 1520 cc
50% of NORMAL
TIME: 10"
EXERCISE
++++ Dyspnea
O2 VENTILATION
5200 cc/min
AIR VENTILATION

FIGURE 10

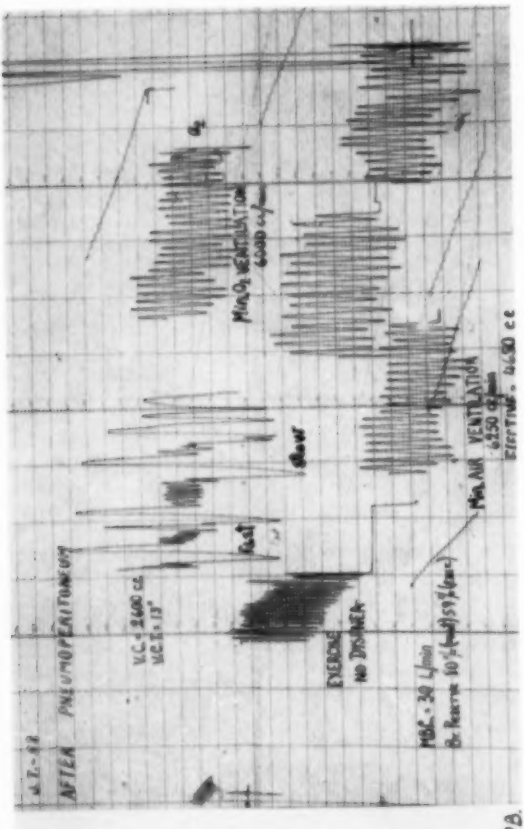

FIGURE 12

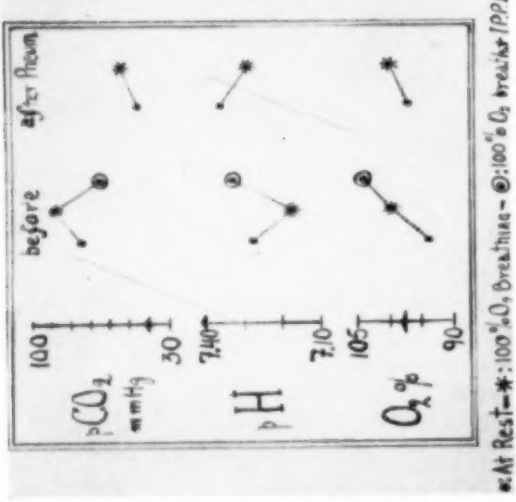

FIGURE 11

were limited. His pulmonary function studies (Fig. 8) showed some of the classical patterns of emphysema: obstructive type of respiration more marked with fast breathing MBC and fast V.C. performance). No hyperventilation was present at rest. Slight dyspnea appears at exercise. The arterial blood values for oxygen pCO_2 and pH are normal. At this stage there is no pulmonary insufficiency but as Comroe points out only pulmonary disability.[1] His dyspnea was due especially to the increased airway resistance.[4, 16] The anatomical damage was just beginning.[15]

Case 9. Intermediate stage of emphysema. A 60 year old man for the last 20 years suffered from mild chronic bronchitis, without asthmatic attacks. He was still able to perform physical work, but dyspnea on exertion curtailed his activities. The chest x-ray films showed clear cut signs of emphysema.

The pulmonary function studies (Fig. 9) presented classic signs of obstructive respiratory insufficiency. There was hyperventilation at rest, somewhat relieved by breathing oxygen, and marked hyperventilation and dyspnea when performing a standard exercise. There was hypoxia at rest and incipient CO_2 retention. The pH was at the lower limit of normal.

The dyspnea was produced by the factors mentioned in the first stage plus the chemical stimulus elicited by hypoxia. It is interesting to note that by teaching him the correct pattern of breathing he was able through voluntary hyperventilation to correct the hypoxia. This has several meanings: it shows that the chemical factor of his dyspnea was not fixed; it calls attention to the derangement of muscular function, and therapeutically, it shows the way toward improving his condition.

Case 10. Final stage of emphysema. A 54 year old railway worker with an inconspicuous history of slight cough was first admitted to the hospital as an emergency case because of spontaneous bilateral pneumothorax, acute pulmonary insufficiency and signs of right heart failure. After the acute stage was over he continued to be dyspneic and had intermittent periods of heart failure. The chest x-ray films showed clear signs of emphysema. No cardiac enlargement was detected. The pulmonary function studies are shown in figure 10. There is obstructive insufficiency of marked degree. As in Case 6 (kyphoskoliosis), despite his dyspnea he was hypoventilating. The results of his ventilatory performance can be seen in the arterial blood values (fig. 11): Hypoxia, marked increase of pCO_2 and respiratory acidosis. Furthermore, one detects an increase in the acidosis by the administration of 100 per cent oxygen breathing ("CO_2 narcosis syndrome").[15, 17]

In this case the dyspnea was the result of all possible factors in emphysema: functional, mechanical and chemical. On top of that there can be no question at this stage of the added factor represented by increased pulmonary artery pressure which already led him to intermittent right heart failure. The moment he lost the compensatory hyperventilation in the wake of chronic CO_2 retention, he entered the truly last phase of the disease. Nevertheless, one should be cautious about this statement because sometimes the signs are reversible. We instituted therapeutic pneumoperitoneum, which reduced considerably his dyspnea by improving the functional performance of his ventilation (Figs. 11 and 12). The cardiac failure subsided and he no longer required digitalization.

SUMMARY

An attempt has been made to utilize the modern concepts of dyspnea producing factors as applied to a variety of cardiac and pulmonary diseases.

1. In the cardiac patients, myocardial failure and pulmonary artery hypertension represent the two primary factors acting, alone or in combination, to produce dyspnea. At the first stage of the disease, both of them may be reversible as a result of conservative or surgical treatment, while their protraction will lead to increased lung rigidity of irreversible nature and permanent dyspnea.

2. In bronchopulmonary diseases, the disturbed mechanical factors of breathing open the stage for dyspnea, while the appearance of pulmonary artery hypertension and heart failure usually represents irreversible damage.

3. Although a good clinical approach is of paramount importance, it is clear that in most dyspneic patients, at least a minimum of relatively simple cardiopulmonary function tests are required for the correct understanding and adequate therapeutic approach. This minimum includes the spirographic record, arterial blood O_2, pCO_2 and pH analysis. For the

evaluation of cardiac dyspnea, the cardiac catheterization is still the most useful tool.

RESUMEN

Se ha intentado utilizar los modernos conceptos de los factores que producen disnea para aplicarlos a una variedad de enfermedades cardiacas y pulmonares.

1. En los cardiacos, el desfallecimiento del miocardio y la hipertensión de la arteria pulmonar, son los dos factores primarios que obran ya sea solos o combinados para producir disnea.

En el primer estado de la enfermedad ambos pueden ser reversibles como resultados del tratamiento quirúrgico en tanto que su prolongación conduciría a un aumento de la rigidez pulmonar de naturaleza irreversible y a la disnea permanente.

2. En las enfermedades broncopulmonares los factores mecánicos perturbados de la respiración abren el cuadro a la disnea mientras que después se establecen la hipertensión de la arteria pulmonar y la insuficiencia cardiaca generalmente irreversibles.

3. Aunque una buena investigación clínica es de primordial importancia, es claro que en los enfermos muy disneicos por lo menos ciertas pruebas de función cardiopulmonar, sencillas, se requieren para la compresión correcta y la terapéutica adecuada.

Este mínimo incluye el trazo espirográfico, el tenor de O_2, pCO_2 y el pH arteriales. Para la estimación de disnea cardiaca la cateterización es aún el método más útil.

RESUME

L'auteur a fait un essai d'utilisation des concepts modernes selon lesquels la dysynée est génératrice de troubles, en les appliquant à une variété d'affections cardiaques et pulmonaires.

1. Chez les cardiaques, l'insuffisance myocardique et l'hypertension artérielle pulmonaire représentent les deux facteurs primitifs agissant, seuls ou en association, pour provoquer la dyspnée. Au premier stage de la maladie, l'un de ces deux troubles traité par un moyen conservatif ou chirurgical, peut être réversible, tandis que l'existence prolongée de ces troubles amènera un accroissement irréversible de la rigidté pulmonaire et une dyspnée permanente.

2. Dans les affections bronchopulmonaires, la perturbation des facteurs mécaniques de respiration ouvre la voie à la dyspnée, tandis que l'apparition de l'hypertension artérielle pulmonaire et d'insuffisance cardiaque représente généralement un trouble irréversible.

3. Bien qu'un examen clinique approfondi soit d'une importance capitale, il est clair que chez la plupart des malades dyspnéiques, il est nécessaire de pratiquer au moins un minimum de tests de la fonction cardiopulmonaire, relativement simples, pour la compréhension correcte de la maladie et de la conduite thérapeutique appropriée. Ce minimum comprend un enregistrement spirographique, l'analyse de la saturation artérielle oxygénée, du CO_2 du sang, et la mesure du pH. Pour l'estimation de la dyspnée d'origine cardiaque, le cathétérisme cardiaque est encore le procédé le plus utile.

ZUSAMMENFASSUNG

Es wurde der Versuch gemacht, die modernen Auffassungen der Dyspnoe erzeugenden Faktoren, wie sie sich beziehen auf eine Mannigfaligkeit von cardialen und pulmonalen Erkrankungen, auszuwerten.

1. Beim Herzkranken stellen das Versagen des Myocards sowie der pulmonale arterielle Hochdruck die beiden Faktoren dar, die allein oder in Verbindung miteinander das Zustandekommen der Dyspnoe bewirken. Im ersten Krankheitsstadium können beide reversibel sein als Ergebnis konservativer oder operativer Behandlung, während ihr protrahierter Verlauf zu einer erhöhten Rigidität der Lunge irreversibeler Natur und permanenter Dyspnoe führen würden.

2. Bei bronchopulmonalen Krankheiten öffnen die gestörten mechanischen Atemfaktoren die Bühne für die Dyspnoe, während das Auftreten von pulmonaler arterieller Hypertension nebst Herzversagen für gewöhnlich eine irreversible Schädigung bedeuten.

3. Obgleich ein gutes klinischen Vorgehen von überragender Bedeutung ist, ist es klar, dass bei den meisten dyspnoeischen Patienten mindestens ein Minimum von relativ einfachen cardiopulmonalen Funktionsproben erforderlich ist für ein korrektes Verständnis und ein zweckmässiges therapeutisches Vorgehen. Dieses Minimum umfasst Spirogram, arteriellen Blutsauerstoff, pCO_2 und pH-Analyse. Zum Zwecke der Bestimmung der cardialen Dyspnoe ist die Herzkatheterisierung noch das nützlichste Instrument.

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Diuretic Therapy

Introduction:

The treatment of edema is one of the common challenges presented to the practicing physician. Excess retention of sodium and water is associated with a number of pathological conditions and is, therefore, the target of various modes of therapy. Diuretic agents are a valuable addition to our therapeutic armamentarium through their ability to block the reabsorption of sodium and water in the renal tubules. However, these drugs do not cure the disease states associated with edema, and consequently the basic measures necessary to correct the underlying pathology should be used when such are available.

In general there are four groups of diuretics in common use today:

1. Organomercurials: The mercurial diuretics when given parenterally are the most potent agents available. They have minimal side effects and produce a persistent diuresis and natriuresis. The mode of action is enzyme inhibition in the renal tubules. Debate still exists as to whether they primarily inhibit chloride or sodium tubular reabsorption. The mercurials when given orally are effective in the higher dose range but gastro-intestinal disturbances are rather prominent limiting factors. Parenterally administered mercurials are quite effective in the acute phase of therapy and are efficient for maintaining the edema free state.

2. Benzothiadiazine Derivatives: The addition of this group of diuretics has been a major advancement in the treatment of edema. Chlorothiazide has had a large clinical trial in the short time since its introduction and has proven to be the most effective oral diuretic at the present time. The drug has a low incidence of dermatologic and gastro-intestinal side effects. The specific mechanism of action in vivo is not known but a rather effective loss of sodium, chloride, bicarbonate and potassium is stimulated. In vitro studies reveal a definite carbonic anhydrase inhibiting effect which does not explain the diuretic response seen in clinical application. Refinement of the activity of chlorothiazide is being investigated by altering the basic structures of this drug. Several other drugs are now ready for clinical distribution which have a variation of the basic structure. Hydrochlorothiazide differs by the addition of 2 hydrogen atoms to the unsaturated double bone of the heterocyclic ring and trifluoromethylthiazide (Flumethiazide) differs by replacing the chloride atom by a tri-fluoromethyl group. These agents are potent diuretics but differ from chlorothiazide in certain features. Hydrochlorothiazide has a similar saluretic effect as chlorothiazide but it has a rather marked chloruretic effect greater than the sodium excreting capacity. The dose of hydrochlorothiazide necessary to produce an equivalent sodium loss as chlorothiazide is approximately one tenth that of chlorothiazide. Therefore 200 mg. of hydrochlorothiazide is equivalent to 2,000 mg. of chlorothiazide. These are the maximum

effective doses of these 2 drugs. Flumethiazide differs from chlorothiazide in its decreased saluretic effect. The dose range of this agent is the same as chlorothiazide since their natriuretic effects are similar at the same dose level.

In the description of treatment of the common edematous states which follows in this paper hydrochlorothiazide and Flumethiazide may be used interchangeably with chlorothiazide if a similar dose of Flumethiazide is used and one tenth the dose is used for hydrochlorothiazide.

3. Carbonic anhydrase inhibitors of the usual sulfonamide variety: The carbonic anhydrase inhibitors such as acetazolamide (Diamox) and ethoxzolamide (Cardrase) have served as efficient diuretic agents in the mild to moderate states of edema with a low incidence of side effects. Their action is inhibition of the carbonic anhydrase of the renal tubular epithelium with resultant depression of hydrogen transport and hydrogen sodium exchange. These agents lose their natriuretic effect in 3 to 4 days and therefore cannot be used continuously. Their loss of effective natriuresis in several days time is unexplained since electrolyte depletion in so short a period of time does not occur.

4. Isocytozine and Xanthine Derivatives: The isocytozine group of drugs such as aminometradine (Mictine) and aminoisometradine (Rolicton) have proved to be effective oral diuretics, but again their efficiency is limited to the mild to moderate states of edema and must be used intermittently to maintain maximum efficiency. The xanthine diuretics such as aminophylline are still in common usage but their potency is poor when compared to the mercurials. However, the combination of the xanthine diuretic with one of the other groups of diuretics frequently potentiates diuresis.

General Administration of Diuretics:

There are no hard and fast rules that govern the use of diuretic agents. The clinical situation will influence the choice of drugs to be used and the mode as well as the dosage with which they will be administered. The difficult case of edema is not only a challenge to our therapeutic ingenuity but is also a test of our knowledge of all the facets of pathophysiology that have produced the state of refractory edema. Concomitant disease such as thiamine deficiency, marked thyrotoxicosis, and anemia, must be ruled out in cases where there is an unsatisfactory response to the therapy. Electrolyte imbalance, which is frequently of iatrogenic origin, may be an important factor in resistance to treatment and when corrected a gratifying diuresis frequently ensues. The terminal stages of myocardial failure may be complicated by anasarca that is associated with severe depression of the glomerular filtration rate and a dilutional hypotremia. Therapy at this point is usually fruitless.

The use of a combination of diuretics frequently is necessary to promote diuresis in the difficult case of edema. For example, the increased glomerular filtration produced by intravenous aminophylline may augment the diuretic response of a mercurial injection. Prolonged mercurial administration results in a hypochloremic alkalosis necessitating the restoration of mercurial action by the use of acidifying salts as ammonium and potassium chloride. The carbonic anhydrase inhibitors produce a hyperchloremic acidosis since their activity promotes a sodium and bicarbonate excretion.

Therefore, the alternate use of a mercurial diuretic with a carbonic anhydrase inhibitor may prolong the diuretic efficiency of both agents. Producing a marked hyperchloremic acidosis by the combined use of ammonium chloride and a carbonic anhydrase inhibitor will increase the chloride load to the renal tubule for a more effective mercurial diuresis. A sodium depletion syndrome resulting from prolonged mercurial or chlorothiazide administration demands the use of intravenous hypertonic saline solution in order to replenish body deficits and present a sodium load to the renal tubule.

Treatment of the Common Edematous States:

When approaching the patient with edema a thorough understanding of the basic pathophysiology is quite helpful in initiating and manipulating the various phases of treatment. Diuretic therapy frequently reverses a number of abnormal factors that contribute to fluid retention but it does not produce a curative effect on the underlying pathology.

Cardiac Edema: In the patient with heart failure there are several mechanisms that are operative in producing salt and water retention through their effects on the kidney. The decreased renal blood flow and glomerular filtration rate of myocardial failure is followed by a decreased sodium and water excretion. A depressed arterial blood flow with increased venous pressure of the liver impairs the inactivation of adrenal cortical salt retaining steroids, such as aldosterone. Further sodium and water retention is fostered by the increased steroid effect on the renal tubules. The hyperosmolarity produced by the electrolyte retention stimulates the hypothalamic osmo-receptors resulting in increased anti-diuretic (ADH) hormone secretion and further water retention. Increased blood volume and venous pressure ultimately produce edema. The basic objectives of treatment are improvement of myocardial function and a reduction of salt and water retention.

When myocardial failure is severe, exercise reduces glomerular filtration farther and there is additional retention of sodium and water. Glomerular filtration is greater in the supine position and therefore, bed rest is quite helpful in aiding diuresis. Prolonged bed rest is fraught with its own particular complications and should be as brief as possible but restricted activity should be advised as a permanent measure. Once the heart has failed it is rare that the cardiac function returns entirely to normal. The more severe the decompensation and the greater the frequency the less chance there is for return toward a normal status. Consequently, maximal therapy is indicated at all times.

Restriction of sodium chloride should always be given primary consideration. Water intake assumes no importance if sodium is rigidly restricted. Frequently a large urinary volume will increase sodium excretion. The more severe the myocardial failure, the less salt can be excreted by the kidney. In mild heart failure restricting the salt intake to 3 grams a day is usually adequate. In moderately severe failure less than 1.5 grams of salt and in severe failure less than 500 mg. of sodium per 24 hour period is essential. With the use of efficient diuretic drugs the sodium intake may be liberalized. Specific dietary instruction is essential for maintaining an adequate sodium restriction.

Digitalis and decreased physical activity are the mainstay of therapy. Through the increased efficiency of myocardial function, as a result of digitalis therapy, a dramatic diuresis may occur. Only when these measures are inadequate are diuretics indicated. Diuretics may be used as follows:

1. In severe heart failure 2 cc. of a parenteral mercurial e.g. meralluride (Mercuhydrin) is given intramuscularly daily for 3 to 5 days until edema has disappeared. Bed rest and digitalization are essential items of this program. In the refractory cases one must be alerted for those factors not remediable by the routine therapy as described, e.g. anemia, thyrotoxicosis, concomitant renal pathology, beri beri, etc.

2. After the decompensation has improved chlorothiazide (Diuril) may be prescribed in a dose of 1,000 mg. every 8 to 12 hours. It should then be reduced to the minimally effective dose which will maintain an edema free state. This is no less than 500 mg. daily since the diuretic activity of this drug would not appear to manifest itself at a dose of less than 250 mg.

3. In the presence of mild heart failure the edema free state may be maintained with acetazolamide (Diamox) 250 mg. or ethoxzolamide (Cardrase) 250 mg. given daily for 3 consecutive days of each week. In moderate to severe failure these agents will rarely be adequate to prevent edema and then chlorothiazide (500 to 1,000 b.i.d.), or chloromerodrin (Neohydrin) 1 to 2 tablets taken orally after each meal and at bed time, can be used to maintain dry weight. When the diuretic must be given parenterally, a mercurial (1 to 4 cc.) may be given as frequently as necessary to prevent fluid retention. With the use of these diuretic agents homeostasis is maintained by reducing the blood volume to a normal level thus decreasing venous return and right auricular filling pressure with an increased cardiac output.

Renal Edema: In the edema of renal disease, as the nephrotic syndrome, there is not only decreased renal blood flow and glomerular filtration rate but there is marked protein loss in the urine. The resultant fall in plasma colloid osmotic pressure is an additional factor in edema production. Therefore, one approach to diuresis is to acutely increase osmotic pressure with an agent such as salt poor albumin. The albumin sometimes appears to have natriuretic and diuretic effects on the kidney which is unrelated to its osmotic activity. Expense may make this procedure impractical. Other factors influencing the edema of nephrosis are increased mineral corticoid and anti-diuretic hormone (ADH) effect on the renal tubule with osmotic shifts of fluids and electrolytes.

The treatment of the nephrotic syndrome initially consists of bed rest, sodium deprivation, and diuretic stimulation with chlorothiazide, 500 to 1,000 mg. twice a day. If these measures are not adequate within one week then a trial with ACTH or steroid therapy is in order. Twenty five milligrams of ACTH in 1,000 cc. of 5% glucose in water given intravenously over an 8 hour period daily for 7 days, or the "gel" given intramuscularly 40 mg. every 12 hours may be tried. Prednisone 10 mg. every 6 hours for 4 doses, then 5 mg. every 6 hours for 8 doses, followed by 5 mg. every 12 hours for 8 doses has also been effective for inducing diuresis. Diuresis

usually occurs when the drug is withdrawn. A complete physiologic or pharmacologic explanation for the effectiveness of ACTH or the steroids in producing the diuresis is not clear. Chlorothiazide may potentiate the diuresis following withdrawal of steroids. If edema is severe, parenteral mercurials may be used with some success without real danger of toxicity from the drug.

Hepatic Edema: In hepatic diseases as in other serious illnesses there are multiple factors accounting for edema formation. Decreased osmotic gradient due to disordered protein formation as well as decreased inactivation of salt retaining steroids and increased ADH production promote a positive sodium and water balance. Portal hypertension is prominent in the phase of ascites formation. No one factor can be incriminated but probably the combination of multiple factors is necessary. In this syndrome the use of intravenous salt poor albumin may be helpful but again the necessary prolonged therapy is quite expensive. The use of a natriuretic agent to combat the increased tubular reabsorption of sodium is frequently helpful and is potentiated by the increased osmolarity produced by administering salt poor albumin. The restriction of sodium intake is essential, and frequently the intake must be less than 500 mg. daily. Bed rest is quite beneficial since hepatic blood flow is greater in the supine position and the demands upon hepatic metabolism are less. A high protein diet to aid in positive nitrogen balance and protein synthesis is effectively utilized unless ammonia intoxication becomes clinically significant. Meralluride (Mercuhydrin) given intramuscularly, 2 cc. daily, will frequently produce marked natriuresis and diuresis when edema is marked and dry weight may be maintained by 500 to 1,000 mg. of chlorothiazide given (Diuril) daily. Occasionally the simultaneous use of mercurial diuretics and chlorothiazide are more effective than when one agent is given alone.

Premenstrual Edema and Edema of Pregnancy: Premenstrual edema is present in 40% of women and is a result of hormonal imbalance. The clinical syndrome consists of weight gain, subcutaneous edema, emotional lability, breast turgidity, anxiety and tension. The hormonal events of the last few days of the menstrual cycle probably influence the renal tubule directly or indirectly with an increased reabsorption of sodium and water. The treatment of premenstrual edema which is usually not marked is as follows:

1. On the last 5 to 7 days of menstrual cycle:
   a. Low sodium diet.
   b. Chlorothiazide in a dose of 500 mg. twice a day or
   c. Acetazolamide (Diamox) 250 mg. (1 tablet) or ethoxzolamide (Cardrase) 125 mg. (1 tablet) daily.

The edema of pregnancy may be an exaggeration of a pre-existing disease as myocardial failure, nephritis, or impending toxemia of pregnancy. During normal pregnancy, the blood volume increases 50% with a positive salt balance reaching a maximum at 36 weeks. Again the common denominator is increased tubular reabsorption of sodium and water which can be blocked in part by appropriate diuretic therapy. Since pre-existing disease may be responsible for edema in pregnancy a thorough medical

survey must be completed. Where there is no underlying pathologic state, then the therapy may be summarized as follows:

1. Low sodium diet when edema first appears.

2. When edema is not controlled by diet; acetazolamide (Diamox) 250 mg. or ethoxzolamide (Cardrase) 125 mg. every other day is prescribed if edema is not marked. When fluid accumulation is more intense, chlorothiazide 500 mg. to 1,000 mg. is given twice a day.

Iatrogenic Edema: Edema as a result of the chronic therapeutic administration of steroids, i.e. cortisone, hydrocortisone, prednisone, etc., is becoming an increasingly more common clinical problem. These agents increase the renal tubular reabsorption of sodium, therefore, the method of therapy is to stop the steroid and promote diuresis. Frequently, it is not possible to stop the steroid and in that case a restricted sodium diet should be used at the onset of therapy. If edema occurs it can usually be treated with 500 to 1,000 mg. of chlorothiazide (Diuril) every eight hours or chloromerodrin (Neohydrin) in a dose of 2 tablets 4 times a day. Occasionally the agents must be used together for adequate results.

Meralluride (Mercuhydrin) given parenterally is quite effective, but must be given every 12 hours since the maximum increase in sodium excretion occurs during the initial 12 hour period after mercurial administration and retention of sodium occurs when the drug is not given again after this period of time.

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ELECTROCARDIOGRAM OF THE MONTH

Retrograde Conduction in Complete Heart Block

The author would be pleased to receive comment and controversy from readers in relation to explanations offered.

This electrocardiogram (Lead II) shows a complete A-V block. The patient had coronary sclerosis without any history of myocardial infarction. Although casual inspection might suggest only 3:1 block, closer study will reveal that the P-R interval gradually lengthens, clearly indicating that total dissociation between atria and ventricles must exist. Furthermore, a ventricular extrasystole appears and it should be noted that the post-extrasystolic pause is as long as the pause between two automatic beats. This proves the presence of complete A-V block. That is, the extrasystole "breaks into" the automatic center on its spread over the ventricles and depolarizes it completely so that impulse formation must begin anew. It is only in complete heart block, when an extrasystole can reach the automatic center, that the post-extrasystolic pause is equal to an automatic period.

The inverted P waves between the QRS and T of the extrasystole and of the first post-extrasystolic automatic beat are also of considerable interest. Such pointed, deeply inverted P waves in Lead II strongly suggest that both the extrasystole and the following automatic beat are conducted in a retrograde direction to the atria. In recent years, study of ventricular extrasystoles in humans has revealed that this occurs much more frequently than previously considered possible. In this patient it is of further interest to find that a ventricular extrasystole and an automatic beat can be conducted in a retrograde direction while there is complete blocking of conduction in the orthograde direction. This situation is all the more remarkable since the retrograde conduction occurs so rapidly; the R-P interval of the extrasystole is only 0.12 second, a short time indeed for conduction in the normal direction. Naturally, an atrial premature contraction arises as a result of the retrograde conduction. If tracings of A-V block are studied carefully, V-A conduction is found not at all infrequently.

The mechanism of such events is unknown. Several theories have been offered. Unidirectional block was assumed to exist; an impulse could travel in one direction but not the other. Activity in a supernormal phase of conductivity was postulated but this idea has little supporting evidence. It has been suggested that the mechanical stimulus derived from the contraction of the ventricle might stimulate an A-V nodal center and induce impulse formation there. We consider it more probable that the activation of the ventricles produces a spread of electrotonic potential beyond the block area as demonstrated with nerve block by Hodgkin, and thus activates the atria. The electrotonic potential created by the activation of the atria is too weak to be able to activate the ventricles beyond the block.

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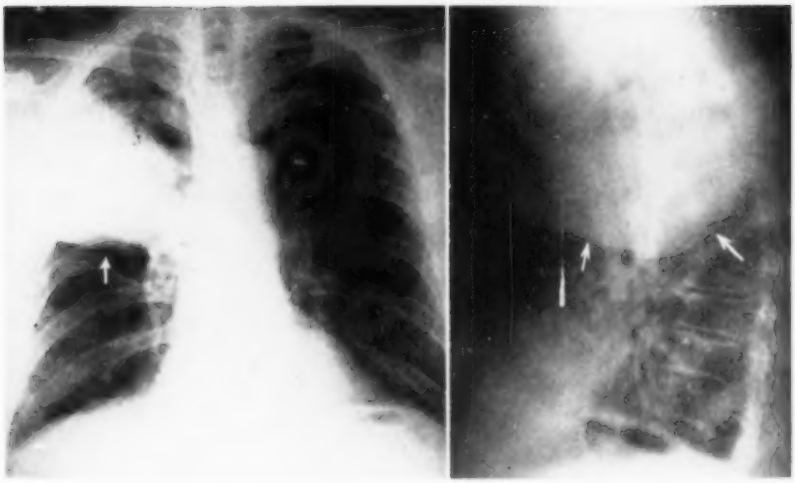
X-RAY FILM OF THE MONTH



Clinical Information

W. K., a 64 year old white man, was admitted to the hospital complaining of shortness of breath and died 31 hours later. Two days prior to admission he developed pleuritic pain over the right upper chest, cough, hemoptysis, chills, fever, and prostration.

Physical examination revealed a very acutely ill patient with temperature 104° F., pulse 120, and respiration 36 per minute. Blood pressure was 100/75. He was deeply cyanotic. There were decreased breath sounds and a few rales over the lower right axilla. The white blood count was 8000 with 84 per cent neutrophiles.

From the admission chest films, shown here, the correct diagnosis was made.

DIAGNOSIS

Friedlander's Pneumonia

Friedländer's pneumonia was suggested roentgenologically, and confirmed by bacterial studies and at autopsy. While the roentgen findings are not pathognomonic, they are highly suggestive of Friedländer's pneumonia. The intense packing of the alveoli with exudate causes considerable enlargement of the affected segment or lobe, resulting in bulging of the adjacent interlobar septa and unusually sharp margins of the pneumonic infiltrate where it does not border on a pleural surface. Abscess formation occurs relatively early. The above findings are seen with greater frequency in Friedländer's pneumonia than in other forms of lobar pneumonia.

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Case Report Section

Varicosities of the Pulmonary Veins:

A Case Report and Survey of the Literature

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Despite extensive references in the literature to various vascular diseases, pulmonary varicosities have been referred to but rarely, and these references have all been isolated case reports. There has been no attempt to demonstrate the feasibility of accurate diagnosis of this condition through present day clinical and radiological facilities. Moreover, no attempt has been made to collect material necessary to establish the prognosis of this disease.

The material dealing with the diagnosis and treatment of pulmonary varicose veins at this time gives no summation of present day information. For this reason this case report and review has been prepared.

A 39 year old colored woman has been observed at the Jewish Hospital in Cincinnati since March, 1948. She was first admitted with complaints of chills, fever, nausea, vomiting, and joint pains. She had had repeated bouts of rheumatic fever since the age of six years.

On physical examination she appeared acutely ill. The major joints were swollen and tender. There was some distention of the neck veins. The lung fields were described as normal on auscultation. Examination of the heart revealed a heaving apical impulse, a diastolic thrill over the entire precordium, and a loud diastolic murmur heard at the apex. Systolic and diastolic murmurs also were heard at the base over the pulmonic and aortic areas. The laboratory reported a normal red cell count and hemoglobin. The white cell count was elevated, as was the percentage of polymorphonuclear cells. The blood sedimentation rate was also elevated. An electrocardiogram was consistent with the clinical interpretation of acute rheumatic fever with mitral stenosis. Further study occasioned by right flank pain led to the clinical diagnosis of polycystic kidneys.

Chest roentgenograms, in addition to the cardiac configuration of mitral stenosis, revealed several densities in the left lower lung field paralleling the left heart border. The main density was a sharply outlined mass measuring 25 mm. in diameter. Clinical investigation for neoplastic or granulomatous disease was noncontributory. On fluoroscopy, however, an observer thought the mass shrank slightly with a good Valsalva maneuver.

By 1952 she had had numerous hospital admissions usually relative to her cardiac condition. The pulmonary densities in question remained unchanged in size and location. An angiocardiogram was performed and demonstrated delayed opacification of the density in question, the density filling with dye after visualization of the main pulmonic arterial tree. Opacification of the lesion was thought to have occurred during the pulmonary venous phase and lasted for six to eight seconds. A guarded diagnosis of an arterio-venous fistula was advanced even though there was no clubbing, cyanosis, or polycythemia. The diagnosis of pulmonary varicosities was later considered when the case was shown at a radiology meeting, and a medical resident in attendance recalled a case report[1] in which a radiographically similar case, without angiocardiography, was discussed.

In 1953 she had developed disabling dyspnea and heart failure. A mitral commissurotomy was performed by one of us (L. G.) in April of that year. In the lingula and extending into the anterior portion of the hilum to involve the superior pulmonary vein, large tortuous blood filled non-pulsating vessels believed to be varicosities were visualized. Biopsy of the auricular appendage showed focal myocarditis.

Her postoperative course was uneventful, and she was discharged June 2, 1953. Since that time she has had no more hospitalizations. She does her own housework and leads a normal life. Recent examination revealed no new physical findings. Clinically her renal status is good. An x-ray film taken in August, 1957 showed this curious density to have remained unchanged in size for almost 10 years.

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On the basis of the angiocardiogram, the appearance at surgery, and lack of clubbing, cyanosis, and polycythemia (which probably would have been present in an arteriovenous fistula), we felt justified in making the diagnosis of pulmonary varices.

Review of the Literature

In the past 50 years only seven cases of pulmonary varicosities have been reported in the literature. The case presented herein is believed to be the eighth. First mention of this condition appeared in the literature in 1907 when Hedinger reported it as an incidental finding at autopsy on a patient who died following surgery.[1] The six other cases were reported between 1923 and 1951. Our case, we feel, is unique in as much as it was

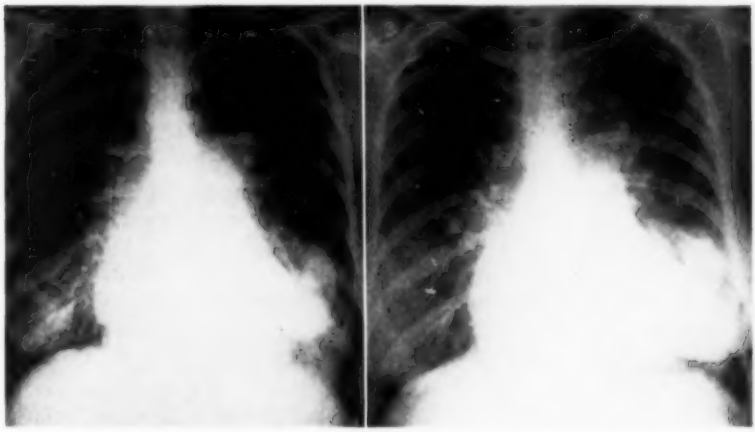

FIGURE 1A FIGURE 1B

Figure 1A: Original chest film taken in 1948. Note lesion along left heart border.—*Figure 1B:* Chest film taken approximately 10 years later.

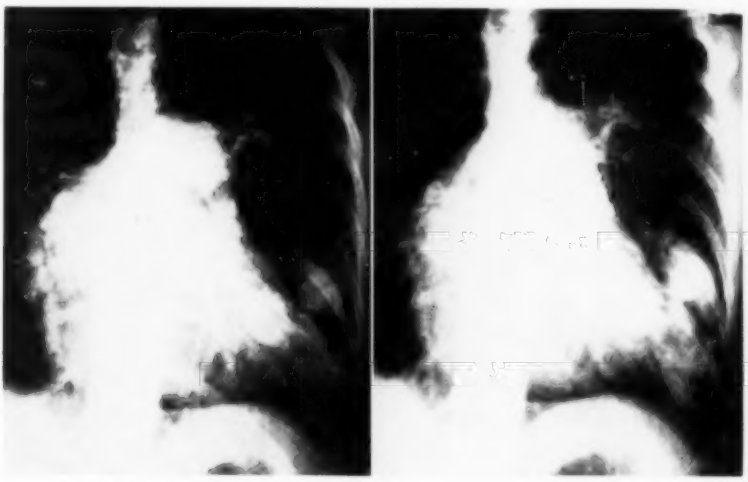

FIGURE 2A FIGURE 2B

Figure 2A: Arterial phase of angiocardiography. The pulmonary artery is filled; the lesion is not yet opacified.—*Figure 2B:* Pulmonary artery phase now completed. The lesion opacifies with the venous phase.

TABLE I

No.	Author	Reported	Age	Sex	Main Symptoms	Associated Conditions	Method Diagnosis Made	Location	Cause of Death
1	Hedinger	1907	44	F	Hemoptysis	Tuberculosis, duodenal ulcer	Autopsy	Left upper lobe	Postoperative complications
2	Nauwerk	1923	45	F	Hemoptysis, epistaxis	Transient hemiplegia	Autopsy	Right lower lobe	Exsanguination
3	Klinck and Hunt	1933	46	F	Severe dyspnea, Retrosternal pain, Clubbing	Hypertension, cardiac enlargement	Autopsy	Left upper lobe (Lingula)	Spontaneous rupture of varix
4	Nieman	1934	57	F	Thoracic pain, weakness, Slight cyanosis, clubbing	Cerebral angiospasm	Autopsy	Left upper lobe	Cerebral encephalomalacia
5	Jacchia	1936	38	M	Hemoptysis	Tuberculosis	Autopsy	Left upper lobe (Lingula)	Miliary tuberculosis
6	Mouquin	1951	36	M	Muscular weakness	None	Angiocardiography	Right lower lobe	(Patient living)
7	Case report Massachusetts General hospital	1951	44	F	Dyspnea, hemoptysis	Mitral stenosis	Autopsy	Left upper lobe (Lingula)	Massive anasarca, malnutrition
8	Gottesman and Weinstein	1957	39	F	Dyspnea	Mitral stenosis, polycystic kidneys	Angiocardiography, surgery	Left upper lobe (Lingula)	(Patient living)

diagnosed preoperatively and verified at surgery. Mouquin's case[5] is the only other case to have had angiocardiography, and to our knowledge is the only other diagnosed case still living. The eight cases are summarized in Table I.

From the table it is of interest to note that all cases fell between the ages of 36 and 57, and all but one are less than 47 years of age. It is also noteworthy that six out of the eight cases were women. Until more information is available it would appear that this condition predominantly occurs in younger adult women.

From the material available it is difficult to state that a definite symptomatology occurs with pulmonary varicosities. Four cases are reported as having had hemoptysis. Of these only Nauwerk's case in 1923 had no associated condition which in itself might have caused the symptom. Three of the patients had presenting complaints of dyspnea, but all three had significant heart disease. In one case the heart disease was hypertensive, and in the other two valvular disease was evident. The question of retrosternal and thoracic pain (Cases 3 and 4) and the appearance of clubbing as reported in the same two cases would on the face of it not seem attributable to pulmonary varices. Certainly, the retrosternal pain in Case 3 could have been on the basis of cardiac enlargement with coronary insufficiency, or any one of a number of causes. It is also remarkable that of the eight cases reported all but three had severe pulmonary or heart disease associated with the varices. Of the associated diseases, two were tuberculosis of a severe degree, and three were advanced heart disease. One, the case being reported, has clinical evidence of polycystic renal disease in addition to acquired mitral stenosis. The two with associated cerebral involvement raise the question of the possibility of cerebral emboli from the pulmonary varicosity. This question was raised in previous case reports. Thrombus formation within the varices was described in the patients who came to autopsy. Only one (Case 6), a French soldier with a presenting complaint of muscular weakness, had no serious disability.

From the radiological standpoint it is significant that six of the eight cases demonstrated left upper lobe lesions with specific mention of lingular disease in four. The remaining two demonstrated the varices in the lower lobe of the right lung.

Review of the causes of death would seem to indicate that in at least three of the cases the pulmonary varices were significant factors. One (Case 4) died of cerebral difficulties which we interpret as intracranial embolization. The other two deaths are more directly due to the varices; Case 2 in which death resulted from erosion of the varix into a first order bronchus, Case 3 in which death was attributed to spontaneous rupture of the varix. These two findings are verified by autopsy reports. A further observation of these cases reported after autopsy (six in all) is that there is no mention of arterial communications. One case report specifically stated that a thorough search for such a communication was looked for unsuccessfully[6].

Differential Diagnosis: In the differential diagnosis of this condition, it is apparent that any pathological entity giving a rounded density within the pulmonary parenchyma demonstrable by roentgenological examination must academically be considered. Rapid approach to differentiation can be

made by classifying the suspect lesion as vascular or non-vascular. It is evident that the non-vascular group includes the granulomata, neoplasms, and cysts (at least those cysts filled with fluid). The bronchial adenoma is an interesting lesion[12] and worthy of mention. Rubin describes it as a tumor affecting young women most often. The left lung is most commonly involved, and the outstanding symptom is hemoptysis. It is not the purpose of this communication to enter into a lengthy and unavoidably repetitious discussion of the clinical picture accompanying any of these various conditions. The usual studies, which may go so far as to include bronchoscopy and a bronchography, may or may not be required dependent upon the clinical picture the particular patient may present.

One of the most important studies in this regard is fluoroscopy with continued examination during Valsalva and Muller maneuvers. This will in almost all cases differentiate a vascular from a non-vascular lesion[11]. Careful observation during these maneuvers will reveal some change in size in the questioned mass in the vascular group of lesions (shrinkage in the Valsalva maneuver; enlargement in the Muller maneuver). The observation of changing size provided the first clue to the diagnosis of the case presented here.

Diseases of the mediastinum and great vessels could possibly create diagnostic problems. The procedures necessary to establish any diagnosis will identify these afflictions as being outside the lungs and militate against a pulmonic vascular abnormality.

The identifiable vascular lesions have been rare, but they deserve mention. Bronchial vein varicosities have been described in connection with mitral stenosis. They are thought to represent the cause of hemoptysis in this condition. These are never seen radiologically[6, 10]. Jack and Lee[8] report an asymptomatic anomalous pulmonary vein. In their case as in several others the anomalies were all in the left lung. Pulmonary artery aneurysm may create a rounded shadow in the hilum but has not been reported within the pulmonary parenchyma.

Attempts at differential diagnosis will inevitably lead to consideration of pulmonary arterio-venous fistula. Between this and the pulmonary varix are several important similarities. The two lesions are indistinguishable by ordinary roentgenologic procedures. Fluoroscopic examination reveals no differences. Age, sex, and associated diseases do not appear to aid in the differentiation. Definitive diagnosis is approached by the clinical findings (Table II) and is established by angiocardiography. Despite the clinical differences between arterio-venous fistulae and pulmonary varices as mentioned in the table, there have been reports of arterio-venous fistulae without physical findings[11]. The case report presented with this review was thought to fall into such a category. Timed angiocardiography helped make the differentiation in this case.

TABLE II

	Clubbing	Cyanosis	Polycythemia	Bruit	Telangectasia
Arterio-venous fistula	Common	Common	Common	Common	Common
Pulmonary varix	2 of 8 cases	2 of 8 cases	None described	None described	None described

The importance of timing has been emphasized by Steinberg[11] who recently reported on 2,239 patients. This group of patients received a total of 3,010 intravenous injections of contrast media with only one death. This review stressed the importance of separate visualization of the arterial and venous pulmonic trees. Mouquin in his case report reached the diagnosis of pulmonary varices by observing "delayed filling" of the suspect lesion. The case reported here further points up the necessity of differentiating between arterial and venous phases of pulmonary vascular filling in angiocardiography. The significance of late opacification of the pulmonary lesion was not originally appreciated but became apparent when the diagnosis of pulmonary varix was advanced.

Comment: Occasioned by identifying pulmonary varices, a search of the medical literature revealed seven other case reports. Recognizing that some of these reports may be open to question, it would appear that pulmonary varices do occur, and when present are demonstrable radiologically. Etiology of this condition has been discussed by Klinck and Hunt[3], and these authors propounded the thesis that the lesions are congenital, and probably insignificant until concomitant disease leads to increasing phlebectasia.

Once visualized, pulmonary varices are difficult to differentiate from asymptomatic arterio-venous fistulae. Timed angiocardiography permits identification. A previous report contains speculation as to treatment.[6] The case reported with this review demonstrated no difficulty stemming from the pulmonary varix either before mitral commissurotomy or since. Cases 2 and 3 were reported in such fashion as to indict the pulmonary varix as the cause of death. In Case 4 it is strongly suggested that cerebral emboli from such a lesion accounted for the demise of the patient.

Until more information is available it would seem reasonable that when pulmonary varices are found, accompanying diseases, if present, should be treated regardless of the varices. Surgical ablation of the varices is feasible, but whether this is indicated is not apparent from the information available.

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A Case of Spontaneous Pneumothorax Complicating Gnathostomiasis*

SOMCHAI BOVORNKITTI, M.D., F.C.C.P. and
SUNTHORN TANDHANAND, M.D., F.C.C.P.

Dhonburi, Thailand

Infections with larvae and immature adults of the nematode *Gnathostoma spinigerum*, acquired by eating raw fish, are of frequent occurrence in Eastern countries:[1] in Thailand recurrent migratory cutaneous swellings are usually pathognomonic of this infection. The parasites have been observed emerging from the skin,[2] and from natural openings such as the vagina and urethral orifice. Some have been picked out or excised from cutaneous nodules or abscesses,[2, 3] others have been found in the abdominal cavity[3, 4] and vitreous chamber of the eye.[3, 5] Although observations of transient pulmonary shadows associated with the condition and of the coughing up of the gnathostomes have been reported,[2, 3, 6] spontaneous pneumothorax as a complication of this disease has not hitherto been described.

M. S., a 33 year old Thai housewife was admitted to Siriraj Hospital on September 3, 1957, with approximately three weeks history of sharp pain and "rippling noise" in the left side of her chest.

She first attended the outpatient clinic on July 14, 1955 complaining of substernal oppression for one week. Physical examination and chest fluoroscopy at that time gave negative results. Subsequently she was seen by us and physicians elsewhere on several occasions with somewhat similar complaints. Chest roentgenogram taken on July 30, 1957, was negative.

About a month before admission she noticed a swelling over her left chest anteriorly accompanied by slight itching and some degree of lancinating pain. Three days later the swelling subsided and five firm discrete cutaneous nodules were noticed in the same area (Figure 1). She then began to feel severe sharp knife-like pain in the left side of her chest anteriorly associated with a peculiar rippling noise on changing position. She also developed productive cough of white tenacious sputum occurring especially when lying on her left side. She was otherwise afebrile and had no other constitutional symptoms. She had frequently eaten raw fermented fish.

On examination she was rather thin, and slightly pale with no apparent sign of distress. Over the left inframammary region four firm discrete cutaneous nodules of about pea size each were observed. They were not tender and the skin overlying them was of normal colour. The chest was clear to percussion and auscultation. All other systems were within normal limits.

The blood picture showed 10,400 white cells per cmm. with 35 per cent neutrophils, 45 per cent eosinophils, and 18 per cent lymphocytes. Stool and urine examinations were non-revealing. Smears of sputum were negative for tubercle bacilli, pathogenic organisms and parasites, but numerous eosinophils were repeatedly noticed; cultures revealed no pathogenic organism. An intradermal tuberculin test (10 T. U.) and several skin tests for gnathostomiasis were strongly positive.

Chest roentgenogram on August 31, 1957 disclosed a moderate degree of pneumothorax with a small amount of fluid in the left hemithorax. Pulmonary opacity was noticed over the left upper lung field (Figure 2A).

During hospitalization she was afebrile. Only slight cough and a small amount of white tenacious sputum occurred when she lay on her left side. This gradually disappeared within a few days without specific treatment. Since the day of admission seven new swellings had appeared on the chest at varying intervals of hours or days, varying in size, location and symptoms (Figure 1).

Biopsy of one of the skin nodules showed a chronic granuloma infiltrated with eosinophils and a few giant cells. Serial blood pictures exhibited persistently high leukocytosis with 35-50 per cent eosinophils. Chest roentgenogram on September 4, 1957 revealed marked clearing of pulmonary shadow and some degree of re-expansion of the collapsed left lung (Figure 2B). Subsequent film on September 18, 1957 showed complete re-expansion of the left lung and the pulmonary shadow was no longer visible (Figure 2C). The patient was discharged on October 1, 1957 apparently in good health.

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Up to January 3, 1958 she had reported three times at the out-patient clinic, each time within two days of a new swelling at a new site, and without any trace of the previous one. All swellings after discharge appeared on the back below the level of the left scapula. Between January 3 and February 25, 1958 no new swelling had appeared.

Discussion

Whereas the lung is the natural habitat of *Paragonimus* (the lung fluke), it is to the nematode *Gnathostoma* but a pathway (and resting place) in its wandering.

Since Levinsen[7] described the first case of human gnathostomiasis in 1889, there have been only a few reports concerned directly with pulmonary lesions. Robert[8] in 1922 mentioned three cases of gnathostomiasis with symptoms related to the respiratory system: the first case with frequent and violent paroxysmal coughs, the second with difficult respiration, and the last case with paroxysmal tenacious coughs. In this country Prommas and Daengsvang[2] noted one patient out of their "Nine Cases" with frequent forced coughing, who subsequently expectorated a male *Gnathostoma spinigerum*. Tansurat,[3] in his recent review of the subject, reported six cases in the category of pulmonary gnathostomiasis: all of them had coughed up worms and exhibited symptoms suggestive of pleuro-pulmonary involvement. In all cases previously reported there was no clearcut evidence of pulmonary invasion except for indefinite chest symptoms and the expectorated worms that might have come from the upper respiratory tract or even from the pharynx. However, Prijyanonda, Pradatsundarasar, and Viranuvatti[6] have added a well proved case of pulmonary gnathostomiasis to the literature.

Almost 10 years ago, in this department, an instance of spontaneous pneumothorax was observed in a patient suffering at the same time from typical recurrent migratory cutaneous swellings of gnathostomiasis.[9] Un-

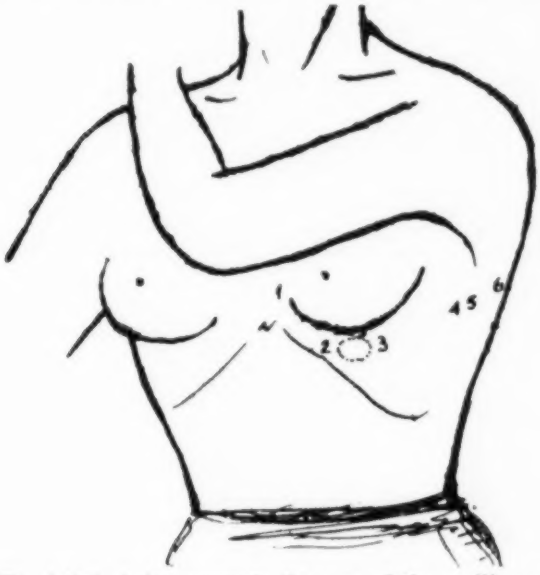

FIGURE 1: The dotted circle represents the area of the swelling while the patient was at home. The numerals indicate the sites of subsequent swellings. The last four appeared on the back.

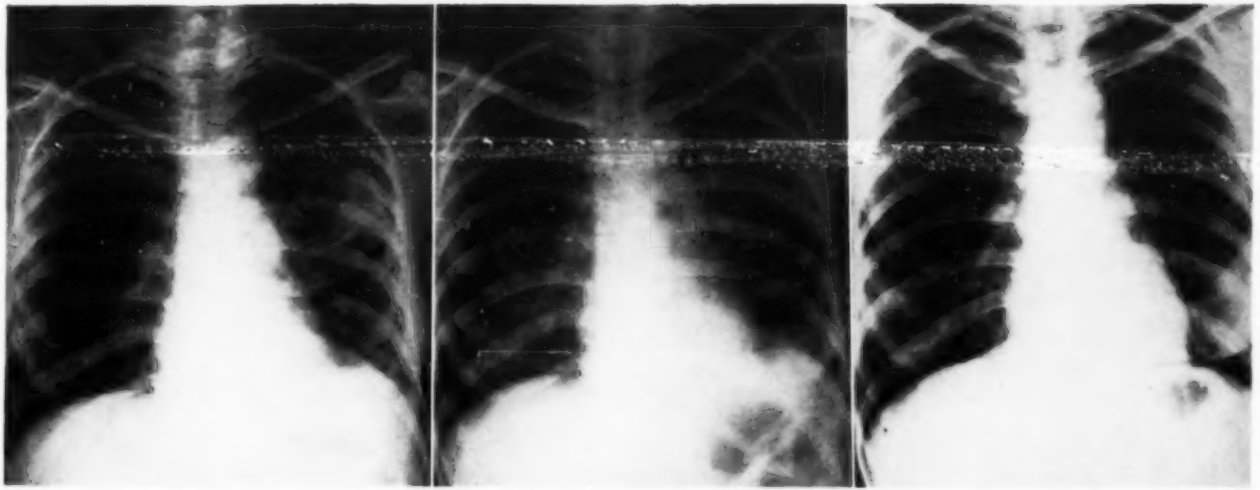

FIGURE 2A FIGURE 2B FIGURE 2C

Figure 2A: August 31, 1957—Moderate degree of pneumothorax, left. Small amount of fluid at left costophrenic angle. Pulmonary shadows, left upper lung field.—*Figure 2B:* September 4, 1957—Some re-expansion of left lung. Marked clearing of pulmonary shadows, left upper lung field.—*Figure 2C:* September 18, 1957—Complete re-expansion of left lung. Pulmonary shadows in left upper lobe no longer visible.

fortunately there was no opportunity to investigate the case further as the patient was not hospitalized and was not followed. To the best of our knowledge, spontaneous pneumothorax occuring simultaneously with *Gnathostoma* infection has not so far been recorded in the literature.

In the case presented here there is little doubt about the diagnosis of gnathostomiasis, a disease characterized by recurrent migratory cutaneous swellings, eosinophilia and positive skin test.

Total disappearance of all swellings after a few days and the absence of any parasite exclude sparganosis. The calabar swellings of loaisis can be excluded both by geographical distribution and by the fact that they are usually much larger than gnathostomal swellings. *Wuchereria malayi*, the only filaria present in Thailand,[10] does not produce subcutaneous swellings.

The transient pulmonary lesions with marked increase of eosinophils in both blood and sputum (Loeffler's Syndrome) in our case indicate local reaction to one or more parasites. Repeated negative results in the search of the sputum for other parasites and the simultaneous presence of subcutaneous swellings, hydropneumothorax and ipsilateral pulmonary lesions are strong evidence of the passage of one or more gnathostomes through the lung and visceral pleura. The sequence of events may have been as follows. The worm entered from the outside, first through the parietal pleura into the pleural cavity where it had freedom of movement and rapidly produced pleural effusion, then on through the visceral pleura into the lung, thus producing spontaneous pneumothorax (and the rippling noise). The somewhat long duration of the pulmonary shadows lends further support to this hypothesis concerning the route of passage of the worm.

The worms that fail to find an exit are supposed to die after a hitherto unknown life span. The longest duration of gnathostomiasis on record is 10 years. This unusually long duration may be explained by repeated infections. Up to February 25, 1958 our patient had had a remission of 56 days from the last occurrence of subcutaneous swellings. She was still free from chest complaint.

Acknowledgment: We are grateful to Dr. P. Tansurat, Section of Parasitology, Department of Pathology, Siriraj Hospital Medical School, Dhonburi, for his valuable information.

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Editorial

The Challenge of the Medical and Legal Professions*

I am highly honored to be your guest tonight—I have so many old friends in the medical profession that I always feel at home talking with doctors. Some of the most interesting hours of my life have been spent with members of your profession, especially when I haven't been the patient.

The accomplishments and success of the many medical societies of your profession have been the envy of the lawyers for years. The membership record of the American Medical Association has been set as a goal for the American Bar Association to achieve. The legal and medical professions are both old and respectable, but if we are to keep our high place in this atomic age, with fast changing conditions, we must work together in unison to meet our common problems in a manner that a short time ago would have been considered impossible.

Doctors and lawyers must always remember that we, in the professions, are a special privileged group—a profession is not a business or a vocation—a profession consists of a dedicated group that is learned in a special field and bound by a code of conduct, which code must require that frequently members of the profession subordinate personal gain for the public good. In recent years both of our professions have learned that we must keep the public informed to avoid unfair criticism of our members and our work. The medical profession has done an excellent job on public information; of course, the average person is more interested in learning of new drugs and new types of surgery than he is in learning of new court rules and new procedures. To explain the history and background of the common law is tedious and complex and makes the legal profession's task difficult.

Medicine and law are big services in our present economy—in 1954 a billion dollars was paid for legal services to about 190,000 lawyers, while about three billion dollars was paid to a few thousand less doctors. Those payments by the public emphasizes the importance of our joint obligation.

Now let me point out briefly what the American Bar Association has done in recent years. In 1954 it dedicated its new Bar Center in Chicago at a cost of approximately Two Million Dollars. In this Bar Center the American Bar Foundation is now functioning and has as one of its most important research projects a survey of the law of mental illness. When this survey is completed, recommendations will be made that should be of great aid in the treatment and care of the people affected with this terrible disease. Over eight hundred thousand of our citizens are now in mental institutions. The Association has fostered a plan for legal aid which makes available legal services to the indigent in most of our larger cities and in many rural areas. New Jersey was the first state to have legal aid available in all of its counties. This program was started in 1949 and

*Presented before the Interim Session, American College of Chest Physicians, December 2, 1957, Philadelphia, Pennsylvania.

since that time many other states have followed the New Jersey plan.

Many Bar Associations have established Lawyer Referral Services, which is low cost legal services for persons in modest circumstances. This service has been widely used by the public and here in Philadelphia is one of the best in the country.

The Courts and the Bar Associations are working constantly to speed the trial of cases so that justice is not denied by delay. More progress has been made in modernizing the courts in the last ten years than in any similar period in our history.

You are so familiar with the free clinics and free services rendered by the hospitals and the medical profession that I shall not dwell on the details, but I do want to mention and congratulate your group on the splendid work done in the field of silicosis. I am sure you already know of the great advancement made by chest physicians in preventing this dreaded disease. I know that your President, Dr. Gordon, was one of the leaders in the research projects that have led to remarkable results. The legal profession cooperated and now we have improved medical treatment as well as new laws and the public have greatly benefited.

It is with temerity that I want to encourage you specialists to take an active interest in the general welfare of the medical profession and the legal profession. Specialization on the part of doctors and lawyers has been greatly accelerated in recent years and has led to the better treatment of certain diseases, but on the other hand, specialization on the part of doctors and lawyers often leads to selfish and narrow thinking. While I am positive that your group is not guilty of this, the following remarks that I am going to make are made with the thought that possibly I can suggest some means by which you may avoid this evil.

A real problem that I think deserves your attention is one of court attendance by doctors in general. You have probably seen the movie—"The Medical Witness," sponsored by our two great associations. This movie, I hope, will go a long way toward helping solve the problem. In spite of all that has been done, there are still many doctors and surgeons who refuse to go to court to testify on behalf of the patient they have treated or operated on. This is so unfair and selfish that I believe the medical societies should take more positive action to correct the evil. Some doctors are so discourteous that they won't have an interview with the patient's lawyer. In many instances, if the interview took place and a comprehensive report given to the lawyer, testimony in court would not be necessary.

If there is any one thing which the lawyers of the American Bar Association learned from our recent visit to London, it was to be more courteous and polite to our fellowmen—not only the British lawyers, but the British people in general made us ashamed of ourselves, that we didn't take time out to be decent and polite in our every day life. If we lawyers and you doctors would be more courteous to each other in our joint relationship, the public would greatly benefit and we should have happier lives.

The Judges of most of our courts treat the medical witness with great respect and make every effort to keep the doctors in court the shortest possible time. Won't you please try to have your societies help solve the

problem so that doctors will not absolutely refuse to go to court. We, in the Bar Association, are trying to eliminate the lawyer or judge who takes advantage of the "honest doctor."

The great challenge to the two professions is—"Can we maintain our independence." England and Scotland have gone a long way toward socialization of the medical and dental professions and have made some progress with the legal profession. We know that with socialization we not only would lose much of our independence, but we should almost have to abandon that "confidential relationship" which exists between doctor and patient" and "lawyer and client." To illustrate that we must always be on the alert to forestall moves toward socialization of our professions, I want to point out that there is now pending in Congress a bill to amend the Social Security Act, which amendment would give three months hospitalization and medical care to all persons receiving social security. It has been estimated that if this amendment should become law, it would cost the Social Security Fund almost four billion dollars and it would be indirectly providing for socialized medicine, but it would not be a bill that would be designated as such.

The American Medical Association and the American Bar Association have been working harmoniously and closely at top level. Charles Rhyne, the President of the American Bar Association, has said the legal and medical professions must collaborate on three major social problems—juvenile crime, mental illness and alcoholism. These problems present a great challenge to the two professions and, unless there is a real joint effort made on the part of both professions, little progress will be made. There are many other matters which should have joint attention, but in my opinion, none of our joint problems will receive proper attention until the rank and file of the doctors and lawyers reach a common understanding and a desire to be helpful to each other—not only for the benefit of the two professions, but mainly for the benefit of the public. If doctors and lawyers go entirely selfish and fail to meet the desires and demands of the general public, then you will see the trend toward socialization greatly accelerated.

It is my belief that joint meetings of doctors and lawyers at the city, county and community level should be fostered in every state in the Union —neither group should attempt to take advantage of the other and there should be developed a real spirit of understanding. Let me tell you that in most of the joint meetings I have attended, the doctors have outtalked the lawyers in every instance—to know people is to understand them. Your group, the American College of Chest Physicians, could very well take a leading part in sponsoring such meetings. It is the duty of both professions to meet this challenge and bring about conditions that will help keep America strong, free and the kind of country we doctors and lawyers want to live in.

We are indeed fortunate that we live under a constitution that is now 170 years old and guarantees us justice and liberty. It is for us to preserve these freedoms and privileges under which we have allowed the creation of a dynamic and wholly new kind of economy—an economy that has resulted in a human well-being without parallel in history or in current times.

We have witnessed many experiments in government throughout the world—we have seen the liberties of the individual subordinated to the power of the State—power in the State creates tyranny where citizens have to be driven to produce.

We can be forever grateful that we live in a nation governed by a written Constitution and the Common Law—doctors and lawyers, by squarely and firmly meeting our responsibilities, can help preserve our freedom and liberty.

By preserving our own strength and independence, we can also help preserve the peace of the world. The atomic and hydrogen bombs have created in the people of the world a great desire for peace which is stronger than ever before in our history. This makes it essential that we strive to fill the gap that exists in civilization's present legal structure so that we can insure peace under law. New legal machinery must be developed, which will maintain national sovereignty, yet still provide for peaceful settlement of disputes between nations under the Rule of Law. To such an end, we should dedicate ourselves so that in the future, our children may live in peace.

ROBERT K. BELL, B.S., LL.B.*
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*Past-President, New Jersey State Bar Association; Member, House of Delegates, Am. Bar Association; Life Member, National Conference of Commissioners on Uniform State Laws.

COMMITTEE ON NOMINATIONS

Elections for offices which will expire in June, 1959, will be held at the Ambassador Hotel, Atlantic City. Recommendations for elective offices may be addressed to Dr. James H. Stygall, Chairman, 1221 North Delaware, Indianapolis, Indiana. The other members of the committee are Drs. Harry Golembe, Liberty, New York and Ray W. Kissane, Columbus, Ohio.

College Chapter News

ALABAMA CHAPTER

The annual meeting of the Alabama Chapter will take place at the Tutwiler Hotel, Birmingham, on April 8. The following program will be presented:

2:30 p.m. "Hyaline Membrane Disease of the Lungs"
Kendrick W. Hare, Birmingham

"Tuberculosis in Children—Today's Problems"
Sarah F. Davis, Birmingham

"Nontuberculous Surgical Chest Lesions Commonly Seen in Children"
Orville W. Clayton, Birmingham

"Bone Marrow Biopsy in Bronchogenic Carcinoma—Preliminary Report"
Richard Dillard, Birmingham

4:30 p.m. Business meeting and election of officers

5:00 p.m. Social hour

ARIZONA CHAPTER

The Arizona Chapter will have a dinner meeting at the San Marcos Hotel, Chandler, on April 30. Guest speakers will be Burgess L. Gordon, Albuquerque, New Mexico and F. Henry Ellis, Jr., Rochester, Minnesota, who will speak on "Current Concepts in Relation to the Emphysema Problem" and "Current Aspects of Cardiovascular Surgery" respectively.

MISSOURI CHAPTER

The annual combined meeting of the Missouri Chapter of the College and the Missouri Trudeau Society will be held at the Hotel Phillips, Kansas City, on April 5. Following is the program:

11:30 a.m. Business meetings

12:00 noon Luncheon

1:00 p.m. "An Analysis of the Prognostic Significance of the Roentgen Manifestations of Lung Cancer"
Thomas E. Keats, Columbia, Missouri

"Prevention and Definitive Treatment of Cor Pulmonale"
Kenneth C. Price, St. Louis

"Newly Recognized Viruses in Acute Respiratory Diseases"
Tom D. Y. Chin, Kansas City, Kansas

"Recent Experiences with Aortic Prosthesis"
Hector Benoit and John H. Mayer, Kansas City, Missouri

"Histoplasmosis—A Review of Recent Developments"
Henry C. Sweany, Mt. Vernon, Missouri

NEW ENGLAND STATES CHAPTER

The spring meeting of the New England States Chapter will be held at the Joslin Auditorium, New England Deaconess Hospital, Boston, on April 4. The program is as follows:

9:00 a.m. Registration
Morning Session—Francis M. Woods, Boston, presiding

9:30 a.m. "Pulmonary Manifestations of Cystic Fibrosis of the Pancreas"
Sidney S. Gellis, Boston

Cardiovascular Case Presentations
Moderator: Walter T. Goodale, Boston

"Management of Thoracic Trauma"
Joseph P. Lynch, Boston

12:30 p.m. Luncheon
Afternoon Session—Irving M. Madoff, Brookline, presiding

2:00 p.m. "Current Use of Pump-Oxygenators"
Elton Watkins, Jr., Boston

Pulmonary Case Presentations
Moderator: Ralph H. Adams, Boston

"Pulmonary Problems in Industry"
Maurice S. Segal, Boston

NEW JERSEY CHAPTER

The New Jersey chapter will present its scientific meeting with the chest section of the New Jersey Medical Society meeting on April 28 in Atlantic City. The following program will be presented:

9:30 a.m. "Open Heart Surgery in the Community Hospital"
Robert Meijer, Monmouth

"The Mechanical Principles of the Heart-Lung Apparatus and Some Physiological Aspects of Extra-corporeal Circulation"
Alfred R. Henderson, Asbury Park

"Sarcoidosis: Clinical and Roentgen Features"
Samuel Cohen, Mario J. Albini, and David Abed, Jersey City

"The Endoscopic Therapy of Parenchymal Tuberculosis"
A. Albert Carabelli, Trenton

NEW YORK STATE CHAPTER

The annual clinical meeting of the New York State Chapter will be held in New York City March 19, 20, and 21 at the Hotel Commodore, College of Physicians and Surgeons of Columbia University, and Roosevelt Hospital respectively. Following is the program:

March 19—Hotel Commodore

8:00 p.m. "Stump the Experts" (Audience is urged to bring problem cases. Five minutes will be allowed for presentation.)
Moderator: Emil A. Naclerio, New York City
Panel: J. Maxwell Chamberlain, Arthur M. Master, Carl Muschenheim, New York City; Henry T. Nichols, Philadelphia; Eli H. Rubin, New York City; David M. Spain, Brooklyn; and Israel Steinberg, New York City

March 20—College of Physicians and Surgeons, Columbia University
Morning Session—Ralph A. Deterling, Jr., New York City, Moderator

9:00 a.m. "The Evaluation of Cardiorespiratory Performance"
Alfred Fishman, New York City

"Bronchography in the Problem Chest Case"
Alexander Crosett, Jr., New York City

"Problems Related to Modern Therapy of Pulmonary Disease"
William Stearns, New York City

"Management of Spontaneous Pneumothorax"
Aaron Himmelstein, New York City

"Treatment of Esophageal Hiatal Hernia"
George H. Humphreys, New York City

Panel—"Open Heart Surgery"
Moderator: George H. Humphreys, II, New York City
Panel: Sidney Blumenthal, Howard Bruenn, Ralph A. Deterling, Jr. and Edgar Hanks, New York City

12:00 p.m. Luncheon
Afternoon Session—Emil A. Naclerio, New York City, Moderator

2:00 p.m. "Management of Thoracic Aneurysms"
Shivaji Bhonslay, New York City

"Surgical Treatment of Acquired Valvular Disease"
F. F. McAllister, New York City

"Diagnosis of Congenital Heart Disease by Phonocardiography"
James Malm and William Rogers, New York City

"Advances in the Management of Chronic Cardiopulmonary Insufficiency"
Alvan L. Barach, Hylan A. Bickerman, and Gustav J. Beck, New York City
"Antibiotic Therapy for Infections of the Thorax"
Charles Findlay, Jr., New York City
"Multiple Papillomatosis of the Bronchi"
Richard Moore and Raffael Lattes, New York City

March 21—Roosevelt Hospital
Morning Session—J. Maxwell Chamberlain, New York City, Moderator

10:00 a.m. "Management of Crush Injuries of the Chest"
Joseph M. Ford, New York City
"Some Observations on Current Radiologic Diagnostic Procedures"
Albert A. Dunn, New York City
"Lesions Simulating Mitral Stenosis"
Charles A. Bertrand, White Plains
"Usual Complications of Resection of Aneurysm of the Thoracic Aorta"
Thomas M. McNeill, New Haven, Connecticut
"Diffuse Mesothelioma of the Pleura"
Walter A. Wichern, Jr., New York City
"Problems Arising out of X-ray Radiation of the Chest"
Henry G. Schaffeld, New York City
"Cavity Formation in Carcinoma of the Lung"
Adrian Lambert, New York City
"Ligation and Division of the Bronchus in the Surgical Treatment of Tuberculosis"
J. Maxwell Chamberlain, New York City

12:00 noon Question and Answer Period

12:30 p.m. Luncheon

OHIO CHAPTER

The annual meeting of the Ohio Chapter will be held in Columbus on April 22 at the Veterans Memorial Building. Following is the program:

2:15 p.m. "Coronary Arteriography"
William Molnar, Columbus
"Pulmonary Capillary Proliferation Induced by Oxygen Inhalation"
Philip Pratt, Columbus
"Differential Diagnosis of Diffuse Pulmonary Disease"
Robert Ebert and John H. Hord, Cleveland
"Respiratory Acidosis"
W. R. Biddlestone, Cleveland

OKLAHOMA CHAPTER

The Oklahoma Chapter will hold its annual meeting on April 19 at the Sequoyah State Park. The program will consist of a consecutive case conference, with cases presented by representatives of the Veterans Administration Hospital, Oklahoma City, the Arkansas State Sanatorium, State Sanatorium, Arkansas, and the University Hospital, University of Kansas Medical Center, Kansas City. Dr. Martin FitzPatrick will represent the University of Kansas Medical Center. In addition, papers on the use of cortico-steroids in tuberculosis will be presented by the Eastern State Hospital, Talihina, and the Western Oklahoma State Hospital, Clinton. Drs. Wendell Hall, Minneapolis and Daniel A. Jenkins, Houston, will discuss the papers.

TENNESSEE CHAPTER

The Tennessee Chapter and Tennessee Thoracic Society will meet jointly in Memphis on April 13. The program is as follows:

12:15 p.m. Luncheon and business meeting

1:30 p.m. "Cytological Studies in the Diagnosis of Esophageal Carcinoma"
Duane Carr, Edward F. Skinner, and John R. Hall, Memphis

"Crushed Chest Syndrome"
Foster Hampton, Jr., Chattanooga
"Tuberculin Testing Program"
Daniel E. Jenkins, Houston, Texas
"Diagnosis and Treatment of Sarcoidosis"
Thomas B. Haltom, Nashville
"Tracheal Fenestration Operation for Pulmonary Insufficiency"
Felix Hughes, James Pate, Roger Campbell, and Wesley Jones, Memphis

TEXAS CHAPTER

The annual meeting of the Texas Chapter will be held at the Hilton Hotel, San Antonio, on April 19. Following is the program:

9:00 a.m. Edward O. Egbert, El Paso, presiding
"Advances in Inhalation Therapy and Other Physical Aids in Treatment of Pulmonary Disease"
William F. Miller, Dallas
"Tuberculous Meningitis in Children"
Patrick I. McShane, Austin
"Physiology of Pulmonary Diffusion in Normal Persons and in Patients with Pulmonary Pathology"
Russell H. Wilson, McKinney
"Pulmonary Alveolar Proteinosis"
Robert J. Carabasi, Temple
Panel discussion: Tuberculin Testing
Moderator: J. Edward Johnson, Austin
Panel: John S. Chapman, Dallas; Austin Hill, Houston; Max Johnson, San Antonio; and Howard F. Smith, Austin

12:30 p.m. Luncheon and business meeting

2:00 p.m. James O. Armstrong, Dallas, presiding
Sixth Charles M. Hendricks Memorial Lecture—"Newer Concepts of the Pathogenesis of the Pneumoconiosis"
Oscar A. Sander, Milwaukee, Wisconsin
"Cor Pulmonale, Its Mechanism and Treatment"
William R. Owen, Houston
"Treatment of Stab Wounds of the Chest"
John Selby, Lubbock
"Surgical Treatment of Bullous Emphysema"
John Kee, Dallas

Book Reviews

THE BACTERIOLOGY OF TUBERCULOSIS, by Darzins, Egons, M.D., University of Minnesota Press, Minneapolis, 1958, $10.00, 488 pages, 54 figures.

This extensive review covers many of the most interesting and important phases of tuberculosis bacteriology. The internal structure of the bacillus is analyzed with the use of light, dark field, phase contrast, ultra-violet, fluorescence, electron and x-ray microscopy, Romanowsky, Feulgen, and other differential staining techniques. The effect on the respiration and growth of the bacilli of different environmental conditions and of the addition of various substances which are added to a basic medium, and the enzymes concerned in their metabolism, are followed by physical and chemical determinations, and by labelling with radioactive isotopes. The collection of sputum specimens with gastric or bronchial lavage or laryngeal swabs, their concentration by alkali and phosphate digestion in a shaker and flocculation with calcium chloride before centrifuging, staining by Osol's technique and cultivation on egg containing solid media are recommended, though other methods, especially fluorescence staining and submerged and dispersed growth in liquid media are given detailed consideration. The determination of the virulence of tubercle bacilli and of the effectiveness of tuberculostatic drugs is presented with extensive observations on the development of lesions in guinea pigs, rabbits, mice, hamsters and incubated eggs. Protective measures are described to minimize the hazards in handling tubercle bacilli.

Emil Bogen, M.D.

TRACHEOTOMY: A CLINICAL AND EXPERIMENTAL STUDY, by Thomas G. Nelson, Major, M.C., U.S.A.R., The Williams and Wilkins Company, Baltimore, Maryland, 1958, $3.75, pp. 111.

This monograph is essentially a composite of articles published previously in The American Surgeon, Vol. 23, Numbers 7, 8 and 9, July, August, and September, 1957. Nonetheless, there is no lack of continuity in its three main divisions: history, clinical aspects, and experimental work.

The historical background of tracheotomy is well documented. The author evaluates changes in indications, attitudes, and in surgical techniques through the centuries. Certain periods were characterized by more rapid advances, and the picture of transition is narrated in an interesting manner.

An evaluation of the indications, technique, and complications encountered in 310 tracheotomies in 300 patients constitutes the major division of the monograph. The patients were all of those who underwent tracheotomy between 1947 and 1955 at Brooke Army Hospital, Fort Sam Houston, Texas. It is admitted that certain selectivity exists that would not make this group a pure random sample, yet the author feels that regardless of an inherent obvious age and sex predominance, the wide range in age plus the diverse indications constitutes a sampling not unlike that of a university medical center.

Indications for tracheotomy are broadly grouped as either "mechanical ventilatory obstruction" or "secretional ventilatory obstruction." The shift of predominance of indication from mechanical to secretional is striking in this series; the latter rises from 0% in 1947 to over 77% in 1955. The great impetus in change is credited to Thomas Galloway's contributions in the treatment and management of the bulbar poliomyelitis patient. Techniques, pitfalls and aftercare are evaluated, including scar deformity. Fundamental to any approach are the division of the thyroid isthmus and the removal of a portion of the anterior tracheal wall for tube placement.

The experimental work consists of an evaluation of types of incisions in cadavers and the study of early and late healing in dogs. The work carried out on cadavers could have been done during the course of tranquil tracheotomies on patients, thereby including the problem of bleeding with a transverse incision in comparison with the longitudinal incision.

This is a thorough and objective summary of the subject matter, reinforced by original contributions embodied in five chapters, containing 47 figures and a reference list of 293 articles and books.

F. L. Lederer, M.D.

Obituaries

RUDOLF LEVY
1900-1958

With the untimely death of Dr. Rudolf Levy, the fight against tuberculosis in Israel lost one of its first pioneers and one of its ablest soldiers.

Dr. Levy came to this country in 1933. Upon completion of his medical studies in Berlin and Wurzburg, Germany, for several years he devoted himself to postgraduate work in the field of tuberculosis with Borchardt, Alexander, Zadek and others. He brought with him a large amount of knowledge and experience pertaining to the clinical and surgical treatment of tuberculosis and combatting tuberculosis as a public health problem.

In 1935 he was put in charge of the most important dispensary of the Anti-Tuberculosis League of Palestine in the then budding Tel-Aviv. Under his able guidance and devotion the modest dispensary developed, during two decades, to be a modern comprehensive chest clinic.

His personal contribution to effective collapse-therapy of this area is without parallel. Dr. Levy was the first physician to perform the Jacobeus-Operation in Palestine, and in the succeeding years the overwhelming majority of these operations all over the country were performed by him. He was consulting physician at most of the tuberculosis institutions at that time—in fact he was regarded as belonging to their staff and performed those strenuous, nerve- and heart-straining operations at regular intervals, sometimes up to 4 or 5 operations a day; always aware of the benefit to the patients, but also of the dangers and potential complications.

Dr. Levy was endowed with a rare combination of fine human qualities. Not only was he an excellent physician and an accomplished master in his

field, devoted to his duty and to the welfare of his patients, but his was the blessed ability too, never to be angry, impatient or intolerant. No one ever heard him raise his voice; he had only friends, no enemies. Above his many duties he found time for scientific activity, teaching and lecturing.

His many patients, his co-workers, his colleagues and friends deeply mourn his loss and will always remember him for his untiring effort to the common good, as a model of a good physician, as an untiring fighter against the white plague, and as a good friend. *Homo humanus fuit.*

J. Weiser, M.D.

JOHN A. SCHINDLER
1903-1957

Dr. John A. Schindler was killed on November 16, 1957 when his car struck a bridge abutment near Monroe, Wisconsin. He is survived by his wife, Dorothea, whom he married in 1928, three daughters and one son.

Dr. Schindler was born at New Glarus, Wisconsin, March 23, 1903. After receiving his bachelor and master of science degrees at the University of Wisconsin in 1926, he studied medicine at Washington University, St. Louis, Missouri. He received his medical degree in 1931. After his internship at the University of Iowa Hospital, he entered private practice in New Glarus.

In 1934 Dr. Schindler and Dr. W. B. Gnagi, Jr. founded the Gnagi-Schindler Clinic at Monroe, Wisconsin, which was later renamed the Monroe Clinic. In 1953 he was appointed by Governor Kohler to a four year term on the state board of medical examiners, from which he resigned in 1956.

Dr. Schindler was a Diplomate of the American Board of Internal Medicine, a Fellow in the American College of Chest Physicians, and a member of the American Trudeau Society.

He became nationally famous in 1949 after his lecture at the University of Wisconsin entitled "How to Live to 100 Happily." His first book entitled "The Old Lead Trail," a history of southwestern Wisconsin, was used as a 7th grade textbook in the Monroe schools. In 1955 he published his best seller, "How to Live 365 Days a Year," for which he received a medal from the Christophers, and in 1956 his second major book, "Woman's Guide to Better Living," was published and became very popular.

Dr. Schindler believed that half the causes of all sickness are mental, caused by worry, anger, and excitement. He was a highly skilled medical man "dedicated to helping people with emotional health problems through the medium of wise and kindly counsel."

He will be greatly missed by his patients, his professional associates, his fellow physicians, but most of all by the members of the Wisconsin Chapter of the College.

Alfred A. Busse, M.D.

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Staff physician wanted immediately for large tuberculosis hospital with modern treatment of tuberculosis and concomitant illnesses. Two week vacation, liberal holiday and sick leave, and attractive retirement program. Ineligible for licensure in Texas need not apply. Salary to $10,600 depending on qualifications. Please address inquiries to Box 300A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Surgical resident wanted July 1, 1959 for tuberculosis hospital, thoracic surgery service, under direction board certified surgeon. One-two years previous surgical training preferred. $300-$400 plus room. Apply: Medical Director, PO Box 1411, Lantana, Florida.

CALENDAR OF EVENTS

NATIONAL MEETINGS

Twenty-fifth Annual Meeting
Silver Anniversary, American College of Chest Physicians
Ambassador Hotel, Atlantic City, New Jersey
June 3-7, 1959

Homecoming Meeting
Silver Anniversary, American College of Chest Physicians
Albuquerque, New Mexico, October 14-17, 1959

POSTGRADUATE COURSES

12th Annual Course on Diseases of the Chest
Philadelphia, March 30-April 3, 1959

4th Regional Course on Diseases of the Chest
Newark, New Jersey, April 1, 8, 15, 22, 1959

CHAPTER MEETINGS

New York State Chapter, New York City, March 19-20
Missouri Chapter, Kansas City, April 5
Alabama Chapter, Birmingham, April 8
Tennessee Chapter, Memphis, April 13
Texas Chapter, San Antonio, April 19
Oklahoma Chapter, Sequoyah State Park, April 19
Ohio Chapter, Columbus, April 22
New Jersey Chapter, Atlantic City, April 28
Arizona Chapter, Chandler, April 30
Florida Chapter, Bal Harbor, May 2
Kansas Chapter, Topeka, May 4
Wisconsin Chapter, Milwaukee, May 5
Mississippi Chapter, Biloxi, May 11
Illinois Chapter, Chicago, May 20

SILVER ANNIVERSARY MEETING

HOTEL RESERVATION FORM

25th Annual Meeting
AMERICAN COLLEGE
OF
CHEST PHYSICIANS

Ambassador Hotel
Atlantic City, New Jersey

June 3-7, 1959

108th Annual Meeting, American Medical Association
Atlantic City, New Jersey, June 8-12, 1959

The Ambassador Hotel, Atlantic City, will be headquarters for the 25th Annual Meeting of the American College of Chest Physicians. Members planning to attend the meeting are urged to make their reservations at once, in order to obtain accommodations at the College headquarters hotel. Please use this convenient order form and mail directly to the Ambassador Hotel.

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American College of Chest Physicians

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26	20,000	Plus	20,000
27	20,000	Plus	16,000
28	20,000	Plus	13,000
29	20,000	Plus	10,000
30	20,000	Plus	7,000
31	20,000	Plus	4,000
32	20,000	Plus	2,000
33	20,000		
34	19,064		
35	18,068		
36	17,042		
37	16,096		
38	15,174		
39	14,260		
40	13,410		
41	12,586		
42	11,794		
43	11,040		
44	10,320		
45	9,634		
46	8,990		
47	8,372		
48	7,798		
49	7,246		
50	6,736		
51	6,254		
52	5,802		
53	5,378		
54	4,982		
55	4,614		
56	4,272		
57	3,952		
58	3,656		
59	3,378		
60	3,122		
61	2,844		
62	2,662		
63	2,460		
64	2,270		
65	2,094		
66	1,932		
67	1,784		
68	1,644		
69	1,518		
70	1,400		

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Last First Middle Initial

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Street City Zone State

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Do you know of any existing impairment in your health or physical condition?

No Yes If Yes—Give Particulars _____

Have you consulted a physician for any illness during the past five years?

No Yes If Yes—Give Particulars _____

I hereby apply for this insurance and agree to pay the annual deposit as specified ($100.00 annually) for the first year and thereafter.
INFORMATION in this application is true and complete to the best of my knowledge and belief. The Company shall incur no obligation because of this application unless and until a Certificate is delivered to the Applicant and the first deposit is made in full while the health or other conditions affecting insurability of the Applicant are as described in this application.

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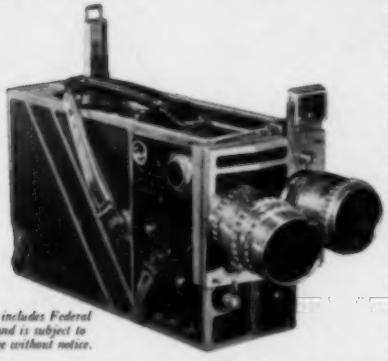

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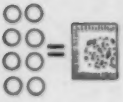

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